LIPOPROTEIN(a) ESTIMATION IN PREMATURE CORONARY ARTERY DISEASE

Dissertation Submitted to

THE TAMILNADU Dr. M.G.R. MEDICAL UNIVERSITY

for

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DEPARTMENT OF GENERAL MEDICINE
COIMBATORE MEDICAL COLLEGE HOSPITAL
COIMBATORE

CERTIFICATE

This is to certify that the Dissertation entitled **" Lipoprotein(a) estimation in premature coronary artery disease"** herewith submitted by **Dr.M.MOHAMED IESA.,** Post Graduate in General Medicine , Coimbatore Medical College to the Tamilnadu Dr. *M.G.R.* Medical University is a record of a bonafide research work carried out by him under my guidance and supervision from Jan 2006 to Jun 2007.

Dr.P.JAMBULINGAM.M.D.,
Professor and Unit Chief

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Dr.K.UMAKANTHAN.M.D.,
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DEAN

DECLARATION

I solemnly declare that the Dissertation titled **" Lipoprotein(a) estimation in premature coronary artery disease ",** was done by me at Coimbatore Medical College & Hospital during the period from Jan 2006 to Jun 2007 under the guidance and supervision of Prof. Dr.K.UMAKANTHAN M.D., and Prof. Dr.P. JAMBULINGAM M.D.,

This dissertation is submitted to the Tamilnadu Dr. *M.G.R.* Medical University towards the partial fulfillment of the requirement for the award of M.D. Degree (Branch *I*) in General Medicine.

Place : Coimbatore **Dr.M.MOHAMED IESA.**

Date :

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INTRODUCTION

Available evidence in literature has shown that Coronary Heart Disease (CHD) is progressively increasing in Indian population and projected to be the number one killer in the next decade (1). Traditional risk factors like smoking, hyper-tension, diabetes are reported to account for only 50% of prevalence and severity of the disease (2). This led to studies on newer risk factors like fibrinogen, Lipoprotein Lp(a), homocysteine, tissue plasminogen activator etc.

The role of lipoprotein(a) [Lp(a)] as a risk factor for ischemic heart disease (IHD) has received considerable attention in recent years. Studies on overseas Indians have shown that Lp(a) is an important risk factor for Coronary Artery Disease. Lp(a) resembles the LDL particle in structure. Apolipoprotein B is the major apolipoprotein associated with LDL; in Lp(a), however, an additional apolipoprotein, apolipoprotein(a), is bound covalently to apolipoprotein B . The physiology and function of Lp(a) are still poorly understood, but the apolipoprotein(a) molecule demonstrates high sequence homology with plasminogen. This suggests that Lp(a) might contribute to the thrombotic, as well as to the atherogenic, aspects of IHD .

Studies on evidence of relationship between Lp(a) and CHD have shown higher levels of Lp(a) in patients than in controls (3-5). Significant relationship of Lp(a) with CHD is reported in South Indian studies (6,7).

The prevalence of dyslipidemia varies by population. Its incidence is highest in patients with **premature CHD**. (CHD before 55 years of age in men and 65 years in women). Lipoprotein Lp(a) excess has been identified as a powerful predictor of premature atherosclerotic vascular disease in several large, prospective studies. Lipoprotein Lp(a) levels modulate the risk of coronary heart disease in patients with hypercholesterolemia, and lipoprotein Lp(a) excess is commonly detected in men and women with premature coronary atherosclerosis. Lp(a) excess increases the risk of premature CHD 3 to 100 fold depending on the absence or presence of concomitant risk factors (8).

Lp(a) levels correlate with both early and advanced atherosclerosis, severity, extent and progression of atherosclerosis and all complications of CHD including re-stenosis following percutaneous transluminal angioplasty, stent and bypass surgery (5).

Study of Lp(a) will help in the process of identifying the risk factors associated with the malignant nature of CHD in Indian population. Also measurement of Lp(a) levels in different populations can help in identifying the high risk group requiring aggressive pharmacological treatment (9, 10). In consideration of the high prevalence of lipoprotein Lp(a) excess in patients with premature coronary heart disease and the intricate role of lipoprotein Lp(a) in atherothrombosis, the present study was undertaken to find out the association of Lp(a) with Premature CHD in a south Indian population from coimbatore.

AIM OF THE STUDY

1. To find out the association of High Lipoprotein (a) levels with premature coronary artery disease patients

2. To find the association of high Lipoprotein (a) levels with the following Risk factors in patients with premature coronary artery disease

1.Systemic hypertension

2.Type 2-Diabetes mellitus

3.Hypercholesterolemia

4.High Low Density Lipoprotein (LDL)

5.Low High Density Lipoprotein (HDL)

6.Hyper-triglyceridemia

7.Smoking

8.Positive family history

REVIEW OF LITERATURE

A. ANATOMY OF CORONARY CIRCULATION

The coronary arteries take origin from the right and left coronary sinuses. In 85% of patient the right coronary artery which gives rise to posterior descending artery supplies the entire right ventricle and large a part of the posterior wall of the left ventricle. This is referred to as right dominant circulation. In 8% of patients the left coronary artery supplies entire left ventricle, interventricular septum and portion of right ventricle. This is referred to as left dominant circulation. In 7% of patients referred to as co-dominant circulation, the right coronary artery supplies right ventricle and posterior wall of interventricular septum while left coronary supplies the left ventricle and anterior portion of interventricular septum.

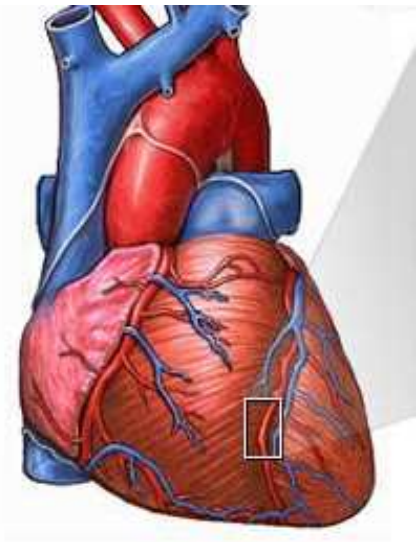


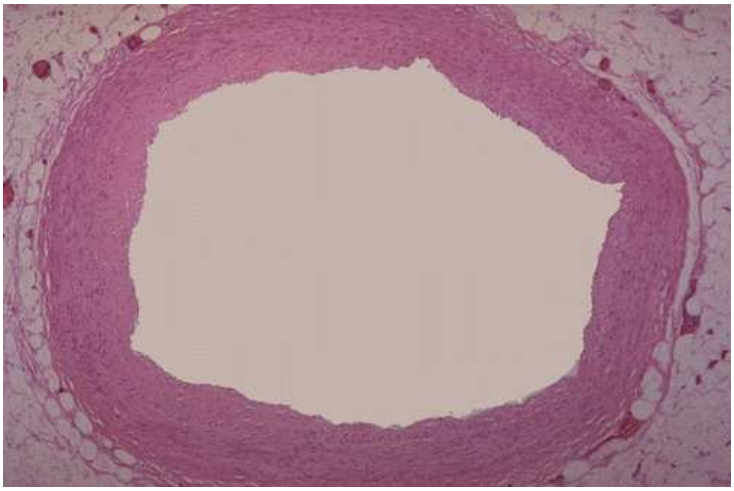
FIG-1: Anatomy of heart and circulation

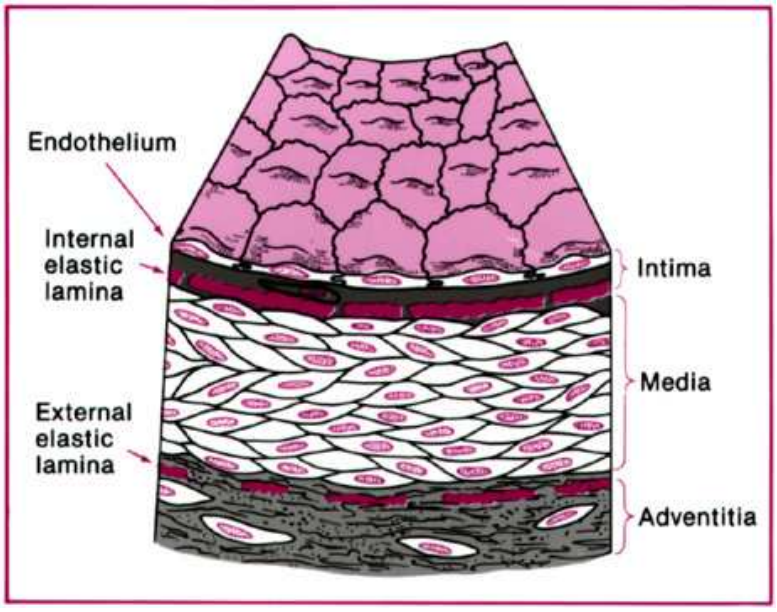
PATHOPHYSIOLOGY OF CORONARY CIRCULATION

The normal coronary circulation is dominated and controlled by the heart's requirements for oxygen. The large epicardial coronary arteries are capable of constriction and relaxation and are referred to as ***conductance vessels***, while the intramyocardial arterioles normally exhibit changes in tone and are therefore referred to as ***resistance vessels*** .Changing oxygen needs of the heart with exercise and emotional stress affect coronary vascular resistance and in this manner regulate the supply of oxygen and substrate to the myocardium (**metabolic regulation**). The coronary resistance vessels also adapt to physiologic alterations in blood pressure in order to maintain coronary blood flow at levels appropriate to myocardial needs (**auto regulation**).

By reducing the lumen of the coronary arteries, atherosclerosis limits appropriate increases in perfusion when the demand for flow is augmented, as occurs during exertion or excitement. When the luminal reduction is severe, myocardial perfusion in the basal state is reduced. Coronary blood flow can also be limited by spasm, arterial thrombi, and, rarely, coronary emboli as well as by ostial narrowing due to luetic aortitis. Myocardial ischemia can also occur if myocardial oxygen demands

Fig-2: Structure of a normal coronary artery:





are markedly increased, and when coronary blood flow may be limited, as occurs in severe left ventricular hypertrophy due to aortic stenosis.

CORONARY ATHEROSCLEROSIS :

Epicardial coronary arteries are the major site of atherosclerotic disease. The normal functions of the vascular endothelium include local control of vascular tone, maintenance of an anticoagulant surface, and defense against inflammatory cells. The loss of these defenses leads to inappropriate constriction, luminal clot formation, and abnormal interactions with blood monocytes and platelets. The latter results in the subintimal collections of fat, smooth-muscle cells, fibroblasts, and intercellular matrix (i.e., atherosclerotic plaques), which develop at irregular rates in different segments of the epicardial coronary tree and lead eventually to segmental reductions in cross-sectional area. When a stenosis reduces the cross-sectional area by ~75%, a full range of increases in flow to meet increased myocardial demand is not possible. When the luminal area is reduced by 80%, blood flow at rest may be reduced, and further minor decreases in the stenotic orifice can reduce coronary flow dramatically and cause myocardial ischemia.

Once stenosis of a proximal epicardial artery has reduced the cross-sectional area by 70%, the distal resistance vessels dilate

Fig-3:Structure of the Endothelial barrier

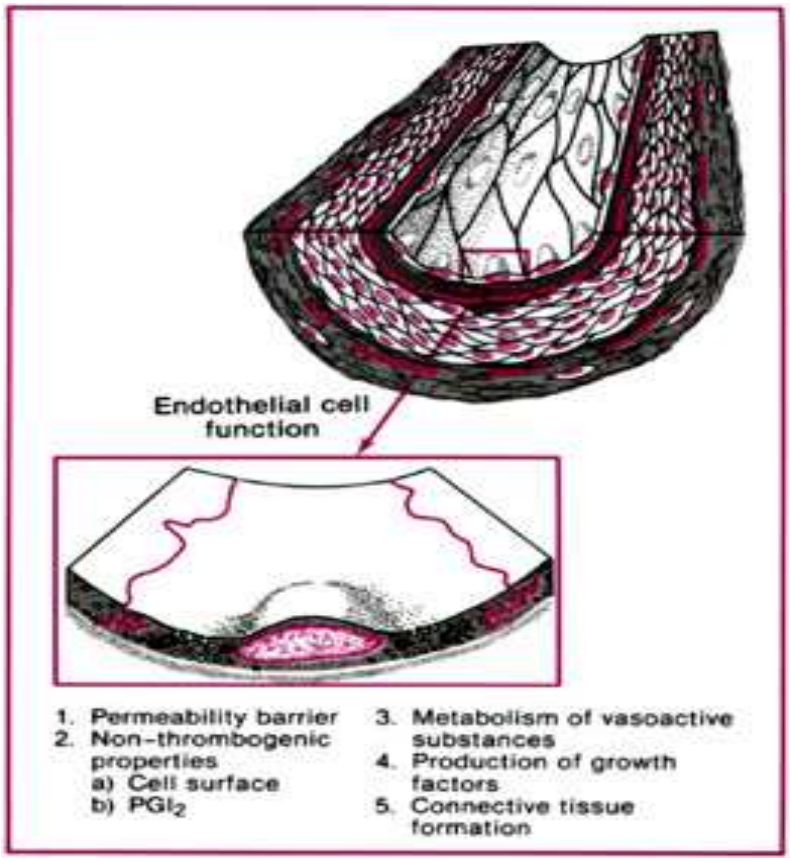
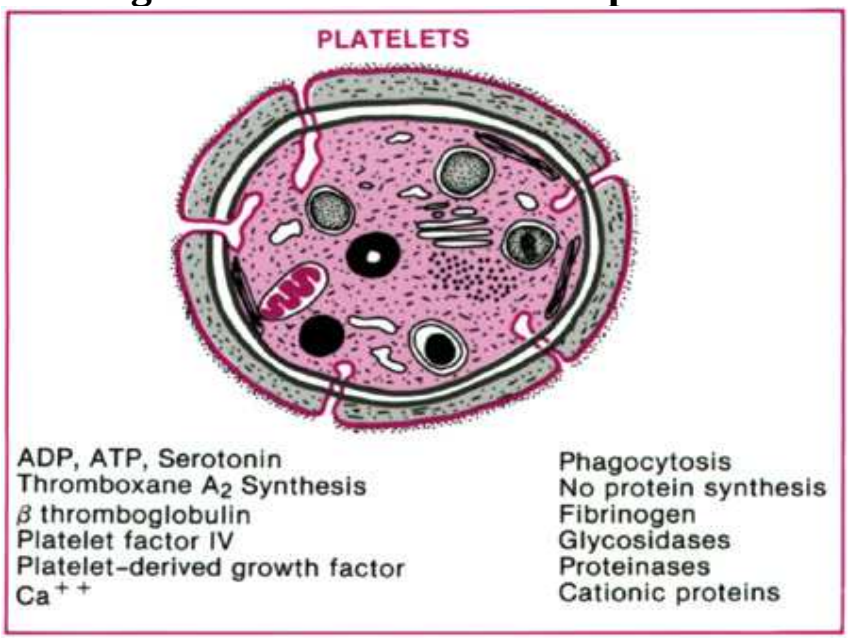


Fig-4:Structure of a normal platelet:



to reduce vascular resistance and maintain coronary blood flow. When the resistance vessels are maximally dilated, myocardial blood flow becomes dependent on the pressure in the coronary artery distal to the obstruction. In these circumstances ischemia, manifest clinically by angina or electrocardiographically by ST-segment depression, can be precipitated by increases in myocardial oxygen demands caused by physical activity, emotional stress, and/or tachycardia.

Stages (phases) of progression of atherosclerosis:

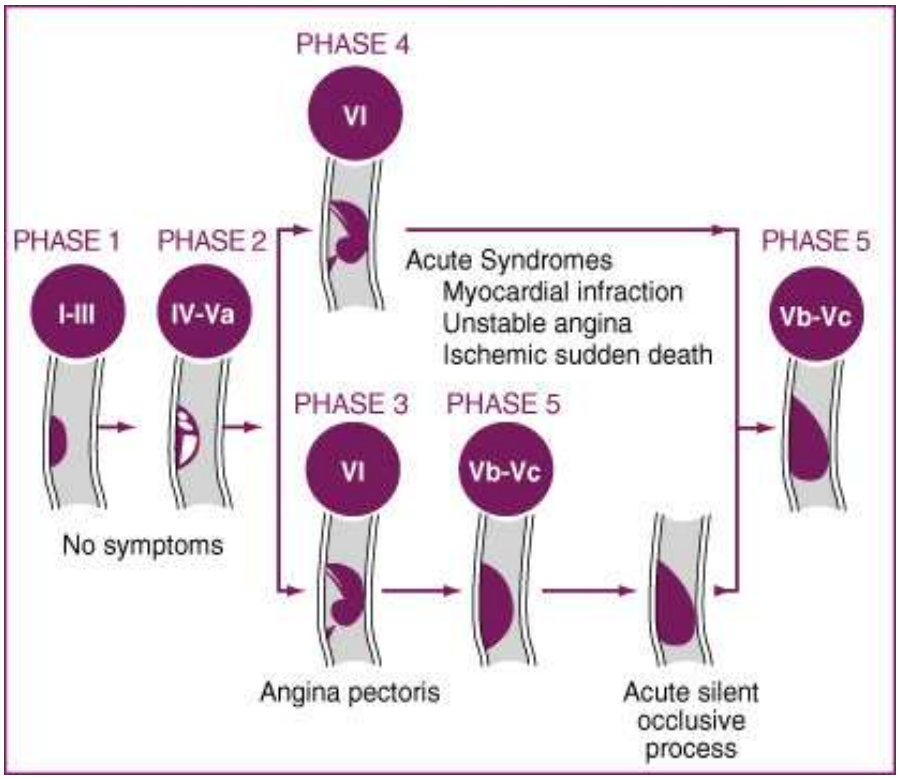
PHASE I TO III: Fatty streak
PHASE IV : Diffuse intimal thickening
PHASEV &VI: Fibrous Plaque

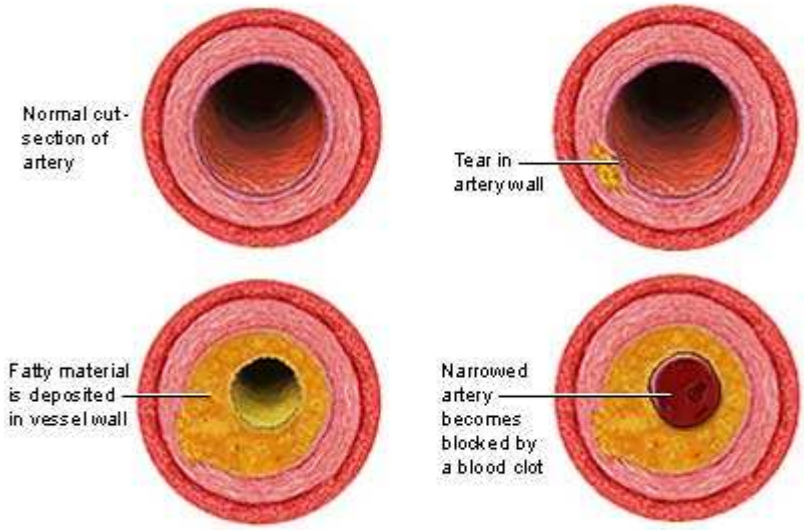
INITIATION OF ATHEROSCLEROSIS

FATTY STREAK FORMATION:

"Fatty streak" observed by *Stary*(11) represents the initial lesion of atherosclerosis. The formation of these early lesions arise from focal increases in the content of lipoproteins within regions of the intima. These lipoproteins bindwith proteoglycan molecules of the arterial extracellular matrix, an interaction that may promote the retention of lipoprotein particles by binding them and slowing their egress from the

Fig-5: Phases of atherosclerosis.





intima. Lipoprotein particles in the extracellular space of the intima, particularly those bound to matrix macromolecules, may undergo chemical modifications that promote atherogenesis: **oxidation and nonenzymatic glycation.**

Diffuse Intimal Thickening : (Lesion Type IV)

Diffuse intimal thickening consists of increased numbers of intimal smooth muscle cells surrounded by variable amounts of connective tissue. These lesions do not progress to advanced lesions of atherosclerosis. These lesions may also have diffusely extracellular lipid intermixed with smooth muscle, macrophages, T cells, and connective tissue.

The Fibrous Plaque (Lesion Types V and VI)

The advanced lesion of atherosclerosis is generally called a fibrous plaque. When the fibrous plaque becomes involved with thrombosis, hemorrhage, and/or calcification, it is often called a complicated lesion.

Fibrous plaques are grossly white in appearance and are usually elevated. In many cases they protrude into the lumen of the artery and, if sufficiently large, compromise the flow of blood. These lesions consist of large numbers of intimal smooth muscle cells, together with numerous macrophages and T-lymphocytes. When the macrophages and smooth muscle contain lipid, the lipid is primarily in the form of cholesterol and cholesteryl ester. The

Fig-6: Surface view of a fatty streak

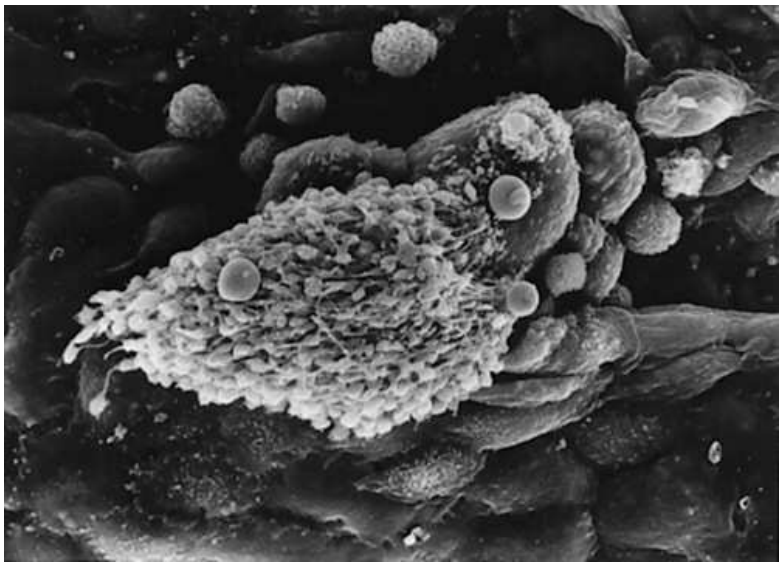
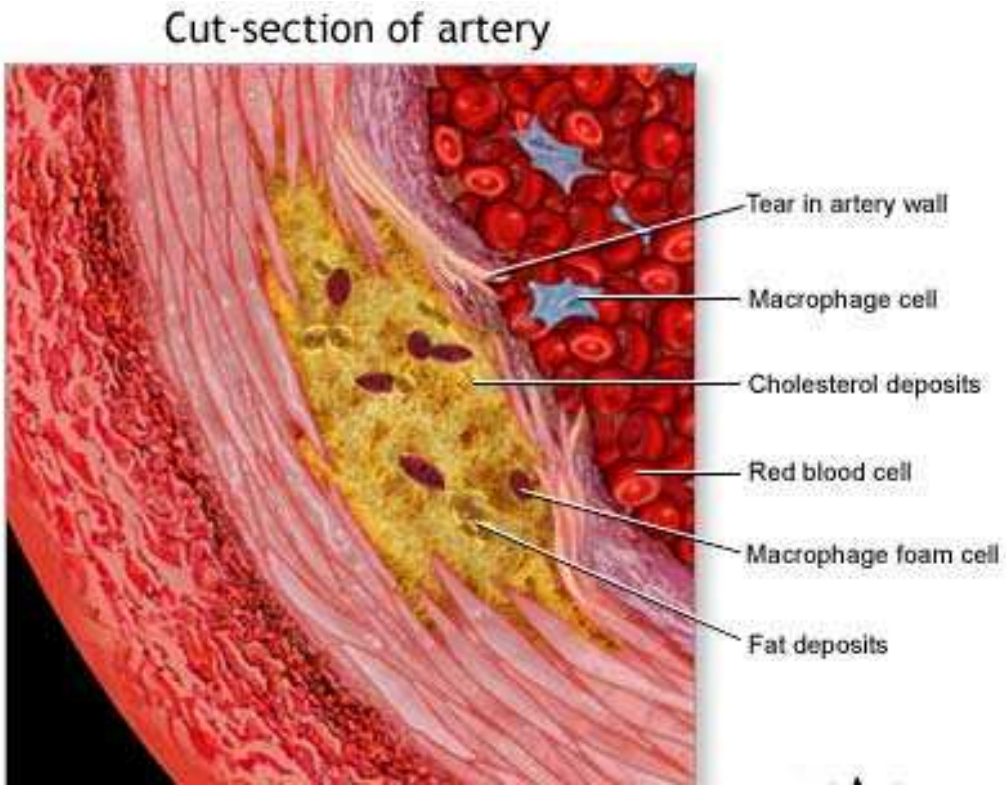


Fig- 7: Structure of a fibrous Plaque



proliferated smooth muscle cells are surrounded by collagen and elastic fibers, by large amounts of proteoglycan, and, in individuals who are hypercholesterolemic, by varying amounts of lipid deposited in the cells and in the connective tissue. Fibrous plaques characteristically are covered by a fibrous cap. The coronary arteries generally demonstrate the most intense involvement, with lesions of atherosclerosis located within the first 6 cm of the artery.(12) The rheological forces play a major role in determining the localization, extent, and severity of lesions in susceptible individuals.(13,14)

Fig-8: Light microscopic view of a fibrous plaque

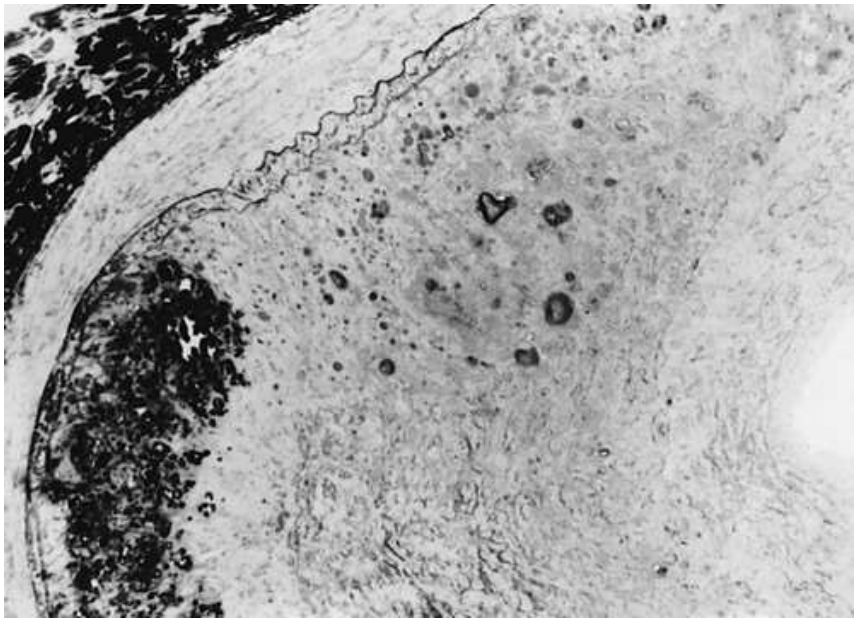


Table-1:RISK FACTORS FOR CORONARY HEART DISEASE:

A. FIXED
1. Age 2. Male sex 3. Family History
B. MODIFIABLE
1. Smoking 2. Hypertension 3. Lipid Disorders 4. Diabetes Mellitus 5.Haemostatic variables 6. Sedentary Life Style 7. Obesity 8. Mental Stress 9. Personality 10. Oral Contraceptive Pills 11. Hyperhomocysteinemia 12. High LP(a) levels 13. Inflammation

1. AGE:

Age is a definite unmodifiable risk factor. Atherosclerosis develops progressively as age advances. Atherosclerosis is rarely present in early childhood, except in familial hyperlipidemia, but it is often detectable in postmortem specimens of young age between 15-30 years. Atherosclerosis is universal in elderly.

2. SEX:

Men are more affected than premenopausal women. However after menopause the incidence of atheroma rises in women. This suggests that oestrogen probably plays a part in preventing or delaying atherosclerosis. There is also a fall in HDL levels in postmenopausal women which may also contribute.

3. FAMILY HISTORY:

Coronary artery disease runs in families. This may be due to genetic factors or the effects of a shared environment (similar diet, smoking habits etc,). A positive family history is generally accepted to refer to those in whom a first degree relative of the patient has developed Ischaemic Heart Disease before the age of 50 years.

SMOKING:

The use of tobacco is one of the primary modifiable risk factors for CAD. Smoking multiplies the effect of other coronary risk factors and is estimated to be the cause of approximately 20 per cent of all deaths of cardiovascular disease .In the Framingham Heart Study, cardiovascular mortality increased 18 per cent in men and 31 per cent in women for each 10 cigarettes smoked per day(15) In addition, the use of tobacco products in individuals with other cardiac risk factors was found to have a synergistic effect on CAD morbidity and mortality. Passive exposure to smoke in individuals who have never smoked may also increase risk for CAD

Smoking may also have a detrimental effect on coronary flow. smoking significantly increased the risk for vasospasm; In addition, it adversely affects endothelial function,(16) fibrinogen level,(17) and platelet aggregation.(18)

HYPERTENSION :

A wealth of epidemiologic data support a relationship between hypertension and atherosclerotic risk, and extensive clinical trial evidence has established that pharmacologic treatment of hypertension can reduce the risk of stroke and heart failure. More recent studies also show a reduction in CHD risk by antihypertensive therapy, particularly interruption of the renin-angiotensin system. In a meta-analysis of nine prospective studies that together included almost 420,000 individuals without prior myocardial infarction or stroke who were followed up for an average of 10 years, baseline blood pressure level correlated with subsequent incidence rates of CAD death and nonfatal myocardial infarction(19). Some studies have found a J-shaped relation between blood pressure and CAD events. In addition, left ventricular dysfunction may affect blood pressure and increase risk for coronary events immediately after a myocardial infarction(20). Large-scale prospective interventional trials are under way to clarify this issue.(21)

DYSLIPIDEMIA:

The major plasma lipoproteins—chylomicrons, very-low-density lipoprotein (VLDL), intermediate-density lipoprotein (IDL), low-density lipoprotein (LDL), and high-density lipoprotein (HDL)—are distinguished by lipid content, density on ultracentrifugation, size, mobility on electrophoresis, and the proteins on their surfaces. The lipoproteins vary in their contribution to atherosclerotic risk: The triglyceride-rich lipoproteins—chylomicrons and VLDL—are not thought to be atherogenic, but the remnants of their lipolysis—chylomicron remnants and IDL, respectively—are believed to be atherogenic. The atherogenicity of LDL—the metabolic end product of VLDL—and lipoprotein(a) [Lp(a)] has been established, as has the cardio protective effect of HDL .

HYPERCHOLESTEROLEMIA:

The dyslipidemia most clearly associated with increased risk for CAD is hypercholesterolemia, particularly elevated plasma levels of cholesterol carried in LDL. LDL contains approximately 70 per cent of cholesterol in the blood and is the primary target of intervention in the guidelines of the second Adult Treatment Panel of the NCEP.(22,23)

The association between elevated blood cholesterol and CAD has been established in observational and interventional epidemiological studies, examples of which are presented here. These data support the lipid

hypothesis: CAD risk is increased at increasing plasma cholesterol levels and can be decreased by decreasing plasma cholesterol.

OBSERVATIONAL STUDIES:

A continuous and graded positive relation was demonstrated between total cholesterol level and CAD mortality in the more than 350,000 men screened for the Multiple Risk Factor Intervention Trial (MRFIT)(24). The relation between total cholesterol level and coronary disease is not limited by nationality or ethnicity, as demonstrated in the Seven Countries Study, which determined that in areas such as Japan and countries surrounding the Mediterranean Sea, where the dietary intake of saturated fat is low and average plasma cholesterol level is relatively low, the mortality rate for CAD is also low, compared with countries such as Finland and the United States, where both the average plasma cholesterol level and the coronary mortality rate are higher(25) Similarly, in the Ni-Hon-San Study, men of Japanese descent living in the United States consumed a diet higher in fat and cholesterol than Japanese men living in Japan(26) and had higher total cholesterol levels(27) and a higher age-adjusted incidence of myocardial infarction and CAD death.(28)

INTERVENTIONAL STUDIES IN PRIMARY PREVENTION:

Randomized, controlled clinical trials have employed a variety of interventions to determine the efficacy of cholesterol lowering in preventing

CAD events in individuals free of known CAD, or primary prevention, and in preventing subsequent CAD events in subjects with known CAD, or secondary prevention.(29)

LIPID RESEARCH CLINICS CORONARY PRIMARY PREVENTION TRIAL.(30)

WORLD HEALTH ORGANIZATION COOPERATIVE TRIAL.

HELSINKI HEART STUDY(31)

OSLO STUDY DIET AND ANTISMOKING TRIAL.(32)

WEST OF SCOTLAND CORONARY PREVENTION STUDY.

INTERVENTIONAL STUDIES IN SECONDARY PREVENTION:

Secondary-prevention trials using dietary, pharmacological, and/or surgical interventions have demonstrated a decrease in the progression of atherosclerotic lesions and a reduction in CAD morbidity and mortality with lipid-regulating therapy.(33)

CORONARY DRUG PROJECT(34)

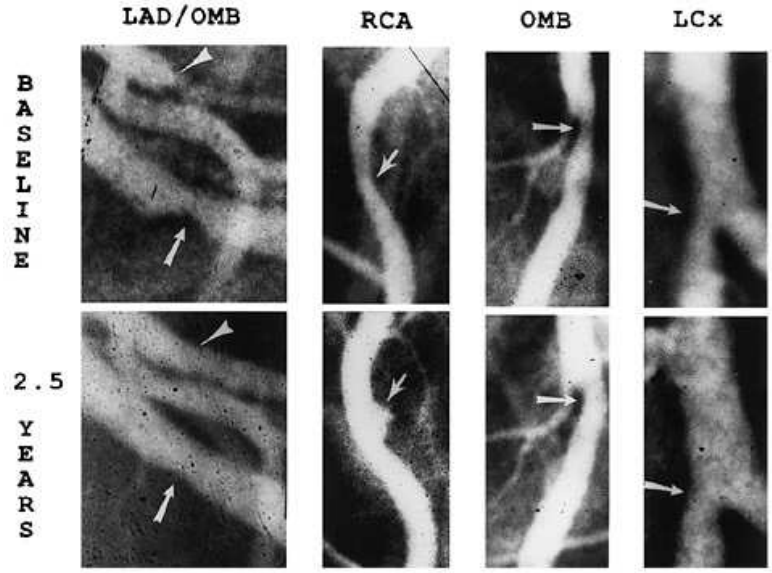
CORONARY INTERVENTION STUDY.(35)

LIFE STYLE HEART TRIAL(36).

MONITORED ATHEROSCLEROSIS REGRESSION STUDY.

CANADIAN CORONARY ATHEROSCLEROSIS INTERVENTION TRIAL.(37)

Fig-9: Regression of atherosclerotic lesions with therapy:



The Current **National Cholesterol Education Panel Adult Treatment Panel III** (**NCEP ATP III)(38)** recommend that all individuals aged 20 years or older without CAD or other atherosclerotic disease have their total cholesterol and, if accuracy can be assured, HDL cholesterol levels measured at least once every 5 years.

The following risk factors (besides LDL cholesterol elevation) are included in the NCEP's algorithm:

Positive risk factors

- Age (45 years or older in men; 55 years or older, or premature menopause without estrogen-replacement therapy, in women)
- Family history of premature CAD (myocardial infarction or sudden death before the age of 55 in father or other male first-degree relative, or before the age of 65 in mother or other female first-degree relative)

- Current cigarette smoking/Hypertension (140/90 mm Hg, or on antihypertensive medication)
- Low HDL cholesterol (<35 mg/dl)
- Diabetes mellitus

Negative risk factor (subtract 1 of the additional risk factors if present)

- High HDL cholesterol (> 60 mg/dl)

Obesity is not included in the algorithm, it should be a target for intervention, as should physical inactivity.

In primary prevention, total cholesterol less than 200 mg/dl is considered desirable

The analysis is performed on a sample obtained after a 12-hour fast to allow clearance of chylomicrons. Total cholesterol, HDL cholesterol, and total triglyceride levels are measured, and LDL cholesterol is calculated by the

Friedwald formula:

LDL cholesterol (mg/dl) = Total cholesterol – HDL cholesterol – (triglyceride/5)

The formula is not accurate if triglyceride is greater than 400 mg/dl or if the patient has type III hyperlipidemia or is homozygous for apo E2; in these instances, LDL cholesterol needs to be determined by ultracentrifugation at a specialized laboratory.

ELEVATED LIPOPROTEIN(a):

Lp(a) level has been shown in a number of clinical studies, primarily retrospective, to be an independent risk factor for CAD.(39) Structurally, Lp(a) is identical to LDL with the addition of a single apo(a) molecule attached by a disulfide bond to the apo B-100. The distribution of Lp(a) concentration is bell shaped in blacks but skewed in whites, who typically have levels below 20 mg/dl. **A level above 30 mg/dl is generally considered elevated**. The primary determinant of Lp(a) level has been shown to be genetic. In one study in white families, more than 90 per cent of the variation in Lp(a) level was attributable to variation in the gene for apo(a).(40) Less than 10 per cent of the inherited variation in Lp(a) level may be attributable to variations in genes at other loci, such as the B/E receptor gene. Lp(a) concentration was reported to be three times higher in patients with heterozygous FH than in controls.(41) About 4 per cent of the variation in Lp(a) level may be attributable to variation in the gene for apo E: Compared with individuals with the gene for apo E3, Lp(a) concentration was 25 per cent lower in individuals with the gene for apo E2 and 25 per cent higher in individuals with the gene for apo E4.(42)

The mechanism by which Lp(a) may increase risk for CAD is complex. Lp(a) may interfere with the generation of plasmin because of structural similarity between apo(a) and plasminogen.(43) Lp(a) has been

demonstrated to be deposited in the arterial wall, particularly in areas with atherosclerotic plaque, and apo(a) has been found co-localized with fibrinogen in the arterial wall.(44) Lp(a) that has been modified by malondialdehyde was reported to be removed by scavenger receptors on macrophages at a rate 20 times higher than that of native Lp(a).(45) Lp(a) appears to be more susceptible to oxidative modification than LDL(46) and thus may be preferentially taken up by scavenger receptors. Although individuals with marked elevations of Lp(a) or homocysteine do appear to have heightened risk of coronary thrombosis, in the population at large these factors show a much weaker correlation with vascular events than LDL, HDL, or the global inflammatory marker C-reactive protein (CRP).

Treatment of elevated Lp(a) is problematic. Most lipid-regulating agents do not seem to lower Lp(a), except, as noted above, nicotinic acid, bezafibrate, and estrogen. Neomycin(47) and stanozolol[48] have also been reported to decrease Lp(a). Although lowering Lp(a) level is theoretically attractive, the clinical impact has not been determined. Because Lp(a) measurement is not a widely available laboratory determination and the clinical significance of alterations in Lp(a) level is not known, the NCEP does not recommend the routine measurement of this lipoprotein at this time.

DIABETES MELLITUS, INSULIN RESISTANCE, AND THE METABOLIC SYNDROME :

Diabetes mellitus is a CHD risk equivalent; most patients with diabetes mellitus die of atherosclerosis and its complications. The abnormal lipoprotein profile associated with insulin resistance, known as diabetic dyslipidemia, accounts for part of the elevated cardiovascular risk in patients with type 2 diabetes. While diabetic patients often have LDL cholesterol levels near average, the LDL particles tend to be smaller and denser and thus more atherogenic . Other features of diabetic dyslipidemia include low HDL and elevated triglyceride levels

The antihypertensive regimen for patients with the metabolic syndrome should include angiotensin-converting enzyme inhibitors or angiotensin receptor blockers when possible. Most of these individuals will require more than one antihypertensive agent to achieve the current American Diabetes Association blood pressure goal of 130/85 mmHg. (49,50,51)

Hemostatic Factors

FIBRINOGEN: Fibrinogen levels vary among populations. Although elevated plasma fibrinogen occurs in conjunction with other CAD risk factors, such as age, cigarette smoking, hypertension, and obesity, fibrinogen has been demonstrated to be an independent CAD risk factor.52 In 6-year follow-up of 2116 men in the PROCAM study, mean plasma fibrinogen

level was significantly higher in men who had coronary events (2.88 gm/liter) than in men who did not have events (2.63 gm/liter), and the incidence of coronary events was 2.4 times higher in subjects in the highest tertile of plasma fibrinogen distribution (>2.77 gm/liter) than in subjects in the lowest tertile (<2.36 gm/liter).(53)

COAGULATION FACTOR VII:

Coagulation factor VII has been shown to increase CAD risk in a number of epidemiological studies.(54) factor VII levels are higher in individuals with a high intake of dietary fat,(55) and a direct association has been established between factor VII and total cholesterol level.(56) Elevated factor VII activity may increase thrombin production,(57) further leading to a hypercoagulant state.

FIBRINOLYTIC ACTIVITY:

Decreased fibrinolytic activity has been reported in patients with coronary atherosclerosis. Studies (58) suggest that the decreased ability to lyse a clot and clear fibrin debris may play a role in atherosclerosis.

PLASMINOGEN ACTIVATOR INHIBITOR :

Decreased fibrinolytic activity may result from elevated levels of PAI-1. In many studies, plasma PAI-1 has been reported to be increased in patients with CAD. PAI-1 was found to be directly related to insulin level, confirming the role of PAI-1 in the insulin-resistance syndrome.(59) In addition to systemic increases in PAI-1, atherosclerotic

lesions have been found to contain higher levels of PAI-1 than the normal arterial wall.(60)

TYPE A PERSONALITY AND STRESS:

The role of personality type(61) and emotional stress(62) in risk stratification for CAD remains controversial. Type A personalities are highly competitive, ambitious, and in constant struggle with their environment, whereas type B personalities are passive and less disturbed by environmental stress. Type A personality was reported to be an independent risk factor for CAD in the Western Collaborative Group Study. Type A subjects were twice as likely to have angina or myocardial infarction as type B subjects.(63) However, in 20 years of follow-up in 1289 men and women in the Framingham Heart Study, there was a significant twofold excess in risk for angina pectoris in both men and women with type A behavior but no association between personality type and risk for either myocardial infarction or fatal coronary events.(64)

FAMILY HISTORY:

Coronary atherosclerosis tends to aggregate in families. In studies that controlled for other risk factors, a family history of CAD has been shown to be a strong independent risk factor for CAD. Although symptomatic CAD typically does not occur until middle age, family history of CAD may influence atherosclerotic risk beginning in infancy (66)

The increased CAD risk associated with a positive family history may be mediated by genetic effects on other risk factors such as obesity, hypertension, dyslipidemia, and diabetes(67). Assessment of family history of these other risk factors may provide additional information about an individual's CAD risk and inform treatment decisions.

ALCOHOL:

The role of alcohol in CAD risk is complicated by difficulties in obtaining accurate data on individual alcohol consumption. In a number of studies, moderate alcohol intake has been associated with decreased coronary risk,(68) and this protective effect may be mediated by an increase in HDL cholesterol.(69) In an analysis of subjects in the Honolulu Heart Program, approximately 50 per cent of the cardioprotection demonstrated with moderate alcohol consumption was attributable to increased HDL cholesterol, and 18 per cent was attributable to decreased LDL cholesterol, although the latter was offset by an increase in CAD risk of 17 per cent caused by increased systolic blood pressure.(70) . Alcohol may inhibit thrombosis(71) and may increase plasma levels of fibrinogen and decrease fibrinolytic activity.(72) Alcohol has been shown to increase tissue-type plasminogen activator (t-PA) secretion by endothelial cells.(73)

In France, CAD incidence is relatively low despite mean plasma HDL cholesterol levels similar to those in other countries and fairly high intake of saturated fat. Suggested explanations for this so-called French

paradox include alcohol-induced inhibition of platelet aggregation(74) and antioxidant effects of red wine.(75)

HOMOCYSTEINE :

A large body of literature suggests a relationship between hyperhomocysteinemia and coronary events. Several mutations in the enzymes involved in homocysteine accumulation correlate with thrombosis and, in some studies, coronary risk. There are no clinical trial data showing that intervention to lower homocysteine levels reduces CHD events

ASSOCIATION OF LP (a) WITH CORONARY ARTERY DISEASE:

Lp(a) is an LDL like particle which has apolipoprotein(a) attached to apolipoprotein B molecule via disulphide bond. There are 34 different Lp(a) isoforms depending on the size of the apo(a). Lp(a) levels are influenced by apo(a) polymorphism. Plasma Lp(a) levels are highly heritable. Stable life long levels are attained by age two. The rate of secretion by liver determines the Lp(a) levels. Ninety percent of the variation in plasma levels is accounted by the apo(a) gene and 70% by the size of apo(a) isoforms (76). Mechanism of **pathogenecity** of Lp(a) excess include enhanced thrombogenesis and impaired fibrinolysis by competing with plasminogen, inhibition of transforming growth factor β, destabilization of

plaque, increased smooth muscle cell proliferation and migration, formation of occlusive thrombus, impaired formation of collateral vessels, enhanced oxidation uptake and retention of LDL-C and upregulation of expression of the plasminogen activator inhibitor (PAI-I) (77-79).

Lipoprotein(a). A **genetic risk factor** for premature coronary heart disease(80)

Lipoprotein Lp(a) excess and premature coronary heart disease(81):

Lipoprotein Lp(a) excess has been identified as a powerful predictor of premature atherosclerotic vascular disease in several large, prospective studies. Lipoprotein Lp(a) levels modulate the risk of coronary heart disease in patients with hypercholesterolemia, and lipoprotein Lp(a) excess is commonly detected in men and women with premature coronary atherosclerosis. Lipoprotein Lp(a) contributes to atherothrombotic risk by multiple mechanisms that include impaired fibrinolysis, increased cholesterol deposition in the arterial wall, and enhanced oxidation of low density lipoprotein cholesterol. Although low density lipoprotein cholesterol therapy to lower lipoprotein Lp(a) may be indicated for patients with premature coronary atherosclerosis, a strong family history of premature atherosclerosis, or refractory hypercholesterolemia. In consideration of the high prevalence of lipoprotein Lp(a) excess in patients with premature coronary heart disease and the intricate role of lipoprotein Lp(a) in

atherothrombosis, this review provides an evidence-based approach to the screening and treatment of patients with lipoprotein Lp(a) excess.

Modification of apolipoprotein(a) lysine binding site reduces atherosclerosis:

Apolipoprotein(a) contains a major lysine binding site in one of its kringle domains. Destruction of this site by mutagenesis greatly reduces the binding of apolipoprotein(a) to lysine and fibrin. Transgenic mice expressing this mutant form of apolipoprotein(a) as well as mice expressing wild-type apolipoprotein(a) have been created in an inbred mouse strain. The wild-type apolipoprotein(a) transgenic mice have a fivefold increase in the development of lipid lesions, as well as a large increase in the focal deposition of apolipoprotein(a) in the aorta, compared with the lysine binding site mutant strain and to nontransgenic littermates. The results demonstrate the key role of this lysine binding site in the pathogenic activity of apolipoprotein(a) in a murine model system.(82)

A prospective study of the role of lipoprotein(a) in the pathogenesis of unstable angina:

This study provides the first evidence in man of a significant role for lipoprotein(a) in unstable angina. The correlation between lipoprotein(a) concentration and cardiac Troponin T concentration suggests that lipoprotein(a) may be significantly involved in the early failure of plaque rupture stabilization.(83)

Contribution of Lp(a) to the occurrence of vascular diseases:

Lp(a) levels in patients with these vascular diseases were especially higher when there were known atherosclerotic risk factors such as diabetes mellitus, hypercholesterolemia or hypertension, although Lp(a) levels in patients with these risk-positive group was not different from that of control. These results suggest that Lp(a) contributes to the development of atherosclerotic vascular diseases especially when known atherosclerotic risk factors are not present. We also investigated the case of thromboangiitis obliterans, which is believed to develop from nonatherosclerotic mechanisms, and found that Lp(a) levels were higher in such patients.(84)

Lipoprotein (a) in the regulation of fibrinolysis:

Elevated plasma levels of lipoprotein(a) [LP(a)] are associated with increased risk of developing atherosclerosis. This increased risk may be due to an Lp(a)-mediated depression of fibrinolytic activity. Lp(a) regulates fibrinolysis by controlling the activity of plasminogen activators. Lp(a) is a low density lipoprotein with an apoprotein(a) subunit which has a high degree of homology with the fibrinolytic zymogen plasminogen. The apoprotein(a) subunit contains up to thirty seven copies of a domain homologous to the plasminogen kringle 4 domain, which enables Lp(a) to bind to fibrin. The subunit also has a zymogen domain, but it is not

activated by plasminogen activators. Lp(a) inhibits plasminogen activation by competing with plasminogen for access to plasminogen activators bound to vascular surfaces. Lp(a) also competes with the irreversible inhibitor of plasminogen activators, plasminogen activator inhibitor-1. Therefore increases in Lp(a) concentration may decrease fibrinolytic activity by preventing activation of plasminogen, but Lp(a) may also prolong plasminogen activation by preventing the irreversible inhibition of the activators. At elevated levels of Lp(a) the decreased rate of plasmin generation may not be offset by the prolongation in plasminogen activation, and fibrinolysis will be inhibited.

Homocysteine and lipoprotein(a) interact to increase CAD risk in young men and women .

Both elevated Homocysteine and elevated Lp(a) showed evidence of being independent risk factors for CAD in men. The presence of both risk factors in men did not appear to confer additional risk. Consistent with prior studies, tHcy and Lp(a) are risk factors, either independently or in concert, for CAD in this clinical population. More significantly, we found evidence that when both risk factors were present in women, the associated risk was greater than what would be expected if the 2 risks were simply acting independently. The absence of such an interactive effect in men may be due to the confounding effects of age manifested as "survivor bias." These

clinical findings provide insights into the potential roles of both tHcy and Lp(a) in the pathogenesis of atherosclerosis.

Social alcohol consumption and low Lp(a) lipoprotein concentrations :

Light or moderate alcohol consumption decreases the risk of coronary heart disease. Beneficial changes in high density lipoprotein cholesterol concentrations are, however, observed at quite high levels of alcohol consumption—that is, ≥20 units per week, 1 unit being 10-12 g. Therefore, other factors may be responsible for decreasing the risk of coronary heart disease when alcohol is consumed in social amounts. The relation between light and moderate alcohol intake and Lp(a) lipoprotein concentrations was studied. Lp(a) lipoprotein is an independent risk factor for coronary heart disease and is affected by alcohol misuse. Study concluded that low Lp(a) lipoprotein concentrations may be one factor explaining low mortality and retarded progression of coronary artery disease in social drinkers. (85)

MATERIAL AND METHODS

Selection of patients:

Coronary heart disease patients of males <55 years and females < 65years (N=100) who were admitted to Coimbatore medical college hospital from January 2006 to June 2007 were recruited for the study based on clinical and electrocardiographic evidence suggestive of coronary artery disease.

An informed consent was taken from all the patients. Patients with chronic liver and kidney disease and acute or chronic infections were not included in the study.

Selection of controls:

Population based controls (N=50), normal symptomatically and electrocardiographically, without the presence of risk factors like smoking , alcohol, diabetes, hypertension, obesity and positive family history were included for this study.

METHODS:

The participants of this study undergo Detailed history with special reference to

1. Age, Sex.
2. Smoking and alcohol habits,

3. Positive family history,
4. History of diabetes,
5. History of hypertension,
6. History of hyperlipidemia,
7. Detailed Physical examination,
8. Anthropometric measurements – includes
    - Waist- hip ratio
    - Waist circumference
    - Body mass index

Fasting blood samples were drawn from all the participants of the study. Total cholesterol, triglycerides and high density lipoprotein cholesterol were estimated using commercial kits on Beckman Cx4 autoanalyzer. Low-density lipoprotein (LDL) was calculated using Friedewald's formula .

LDL cholesterol (mg/dl) = Total cholesterol – HDL cholesterol – (triglyceride/5)

Total cholesterol/HDL-C ratio and LDL-C/HDL-C ratio were calculated.

Serum Lp(a) estimation was performed using quantitative **Latex enhanced immuno-turbidimetric method** using Human Lp(a) kit.

Desirable: < 14 mg/dL

Borderline risk: 14 - 30 mg/dL

High risk: 31 - 50 mg/dL

Very high risk: > 50 mg/dL

Waist circumference more than 95cms for males and 85cms for females BMI > 30, waist hip ratio >0.9 for females and >1.0 for male were taken as obese and high risk for coronary artery disease

High total cholesterol (> 240mg/dl) , High Triglycerides (> 150mg/dl), High LDL ($\geq$ 130mg/dl) and Low HDL ($\leq$ 35mg/dl) were considered as positive high risk factors for coronary artery disease.

Serum Lipoprotein(a) value of **more than 30mg/dl** was taken as high risk factor for coronary artery disease. The mean values of LP(a) and the Lipid profile parameters were calculated among the cases and the controls and were compared. The frequencies of the distribution of each risk factor among the 100 cases were tabulated. The mean LP(a) values in those patients with each of the risk factor and those patients without the risk factors were calculated separately and compared.

Fig-10 :Picture of a lipid profile auto analyzer

OBSERVATIONS

The results and observations of the study are presented below.

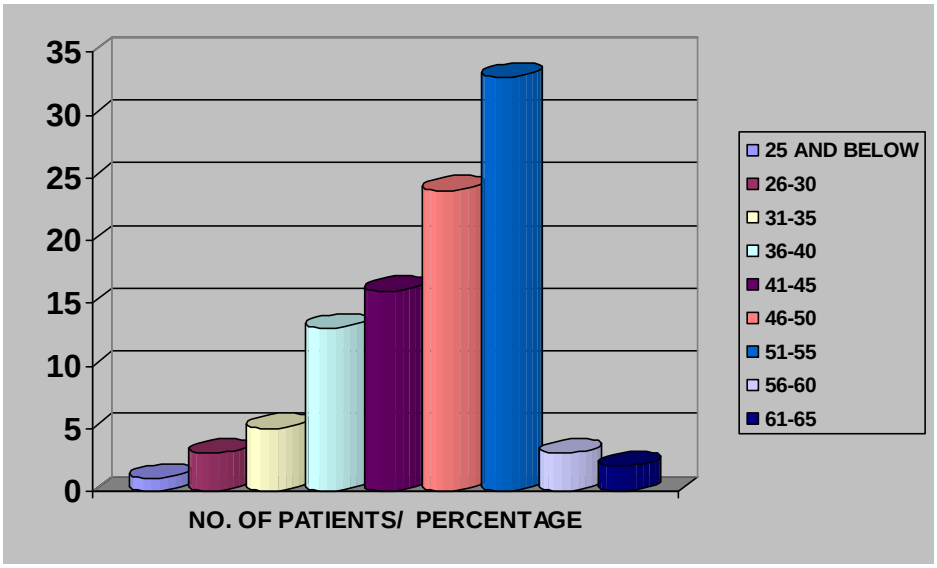
CLINICAL PRESENTATION:

In this study of 100 cases, 95 cases presented with typical anginal chest pain in the retrosternal region which lasted for about 15 min to several hours. Remaining cases presented with atypical symptoms. 32 of them had exertional dyspnea also along with chest pain. In 89 cases, examination of cardiovascular system showed no abnormalities. 9 cases had a loud A2 sound and and ejection systolic murmur in the aortic area probably related to the Atheroslerosis.Two remaining Cases had a pan systolic murmur in the mitral area on auscultation suggestive of papillary muscle dysfunction. Respiratory system examination in 14 cases revealed bi basal crepitations indicative of cardiac failure.

RISK FACTORS ANALYSIS IN 100 CASES OF PREMATURE CORONARY ARTERY DISEASE:

1.AGE DISTRIBUTION: (table-2)

AGE IN YEARS	NO. OF PATIENTS/ PERCENTAGE
25 AND BELOW	1
26-30	3
31-35	5
36-40	13
41-45	16
46-50	24
51-55	33
56-60	3
61-65	2



Male patients of >55 years and female patients of >65 years were excluded from the study .The increased incidence of coronary artery

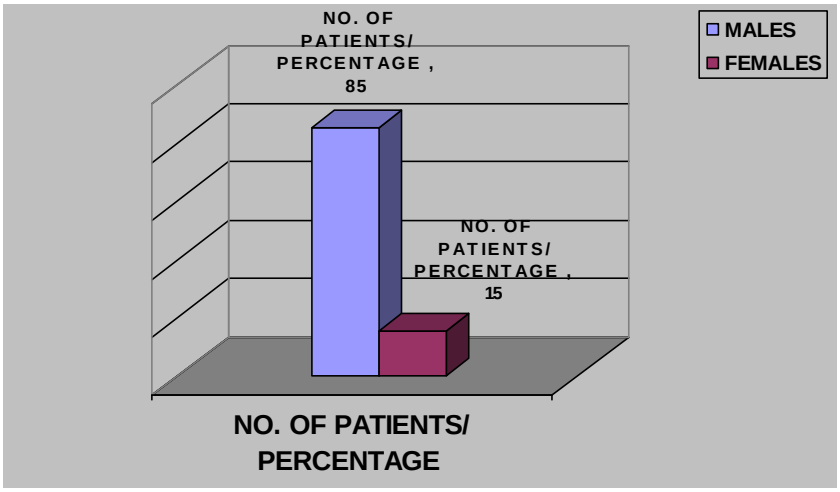
disease in the age group 51 – 55 years is probably related to the age related progression of atherosclerosis.

SEX DISTRIBUTION:

The sex distributions of the 100 cases were tabulated below.

Table-3:

SEX	NO. OF PATIENTS/ PERCENTAGE
MALES	85
FEMALES	15

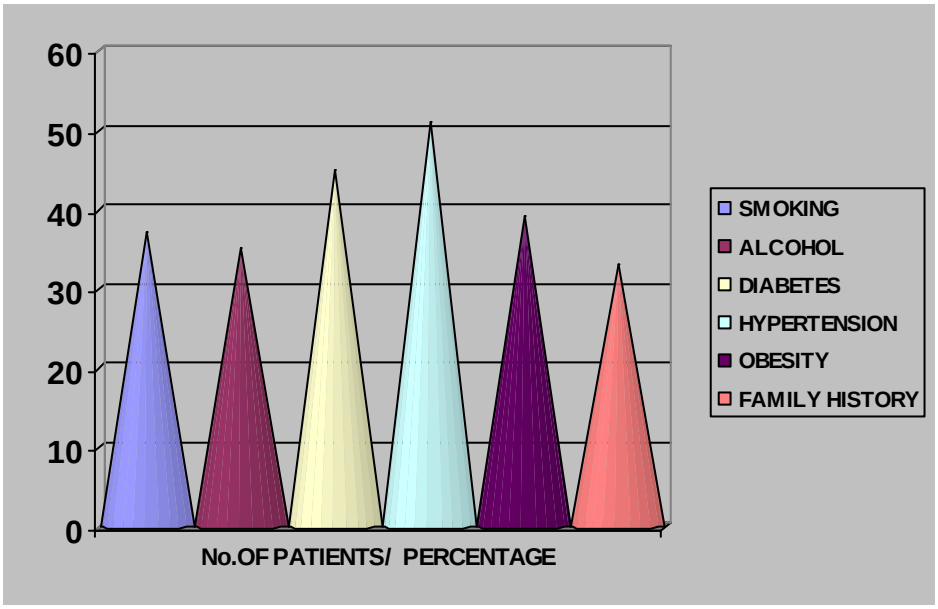


OTHER RISK FACTORS:

The distributions of other risk factors among the 100 premature CAD cases were as follows.

(Table-4)

RISK FACTORS	No.OF PATIENTS/ PERCENTAGE
SMOKING	36
ALCOHOL	35
DIABETES	46
HYPERTENSION	49
OBESITY	39
FAMILY HISTORY	33

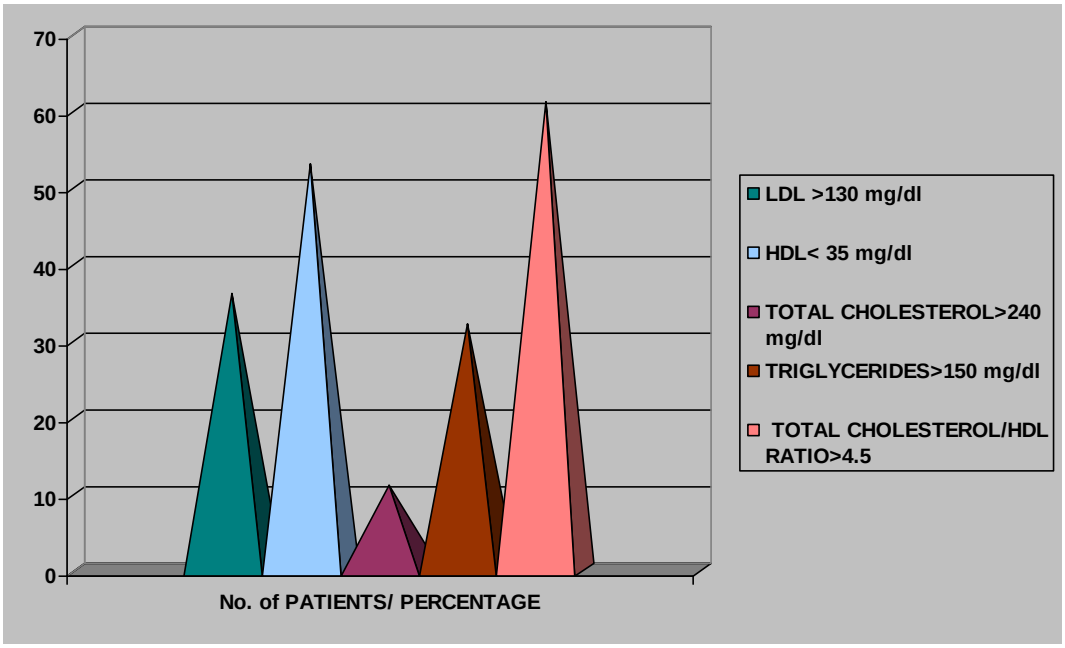


LIPID PROFILE:

The distribution of abnormal lipid profile values among the 100 cases were shown below.

(Table-5)

RISK FACTORS	No. of PATIENTS/ PERCENTAGE
LDL ≥130 mg/dl	36
HDL< 35 mg/dl	53
TOTAL CHOLESTEROL>240 mg/dl	11
TRIGLYCERIDES>150 mg/dl	32
TOTAL CHOLESTEROL/HDL RATIO>4.5	61

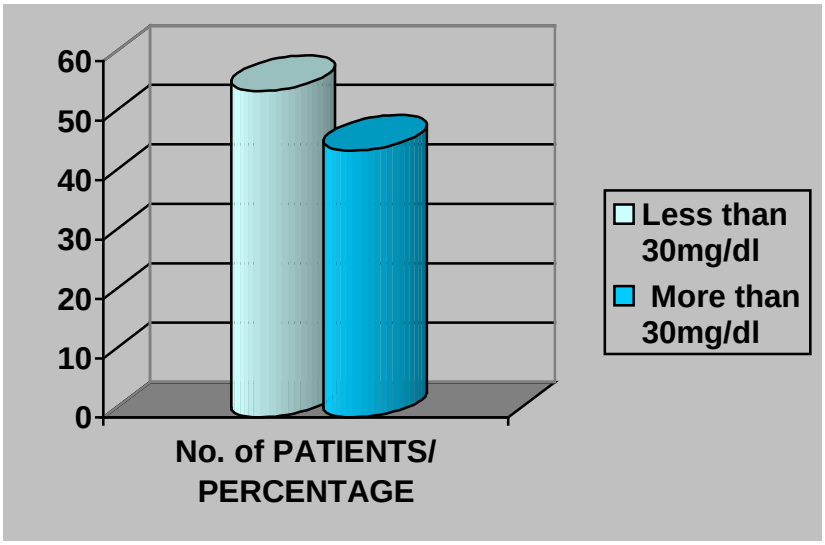


LIPOPROTEIN (a):

The mean Lipoprotein (a) among 100 patients of premature coronary heart disease was found to be **30.98mg/dl.** Among the 100 patients, 46 of them have significantly raised serum LP(a) levels.

(Table-6)

SERUM LP(a) mg/dl	**No. of PATIENTS/ PERCENTAGE**
Less than 30mg/dl	54
More than or equal to 30mg/dl	46

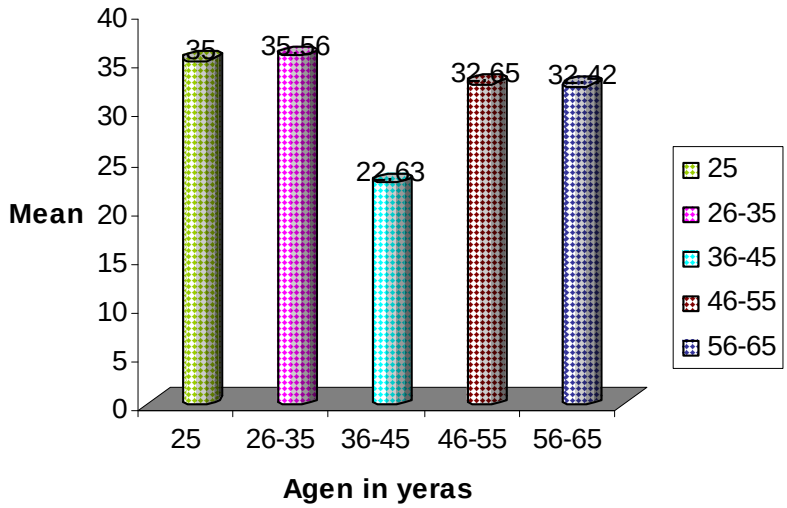


SERUM LP(a) CONCENTRATION IN DIFFERENT AGE GROUPS:

The mean serum Lipoprotein (a) values in different age groups of premature CHD patients are as follows.

Table-7:

SL.NO	AGE IN YEARS	MEAN LP (a)mg/dl
1.	<25	35
2.	26-35	35.56
3.	36-45	22.63
6.	46-55	32.65
8.	56-65	32.42

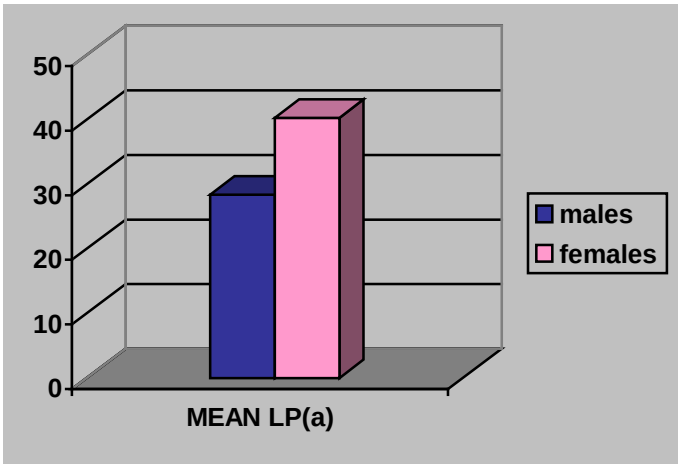


SEX DISTRIBUTION:

The mean serum Lipoprotein (a) values among the male and female Premature CHD patients is as follows. Higher Lipoprotein (a) levels were observed in female sex

Table-8:

SL.NO	SEX	MEAN LP(a)mg/dl
1.	males	28.42
2.	females	40.3

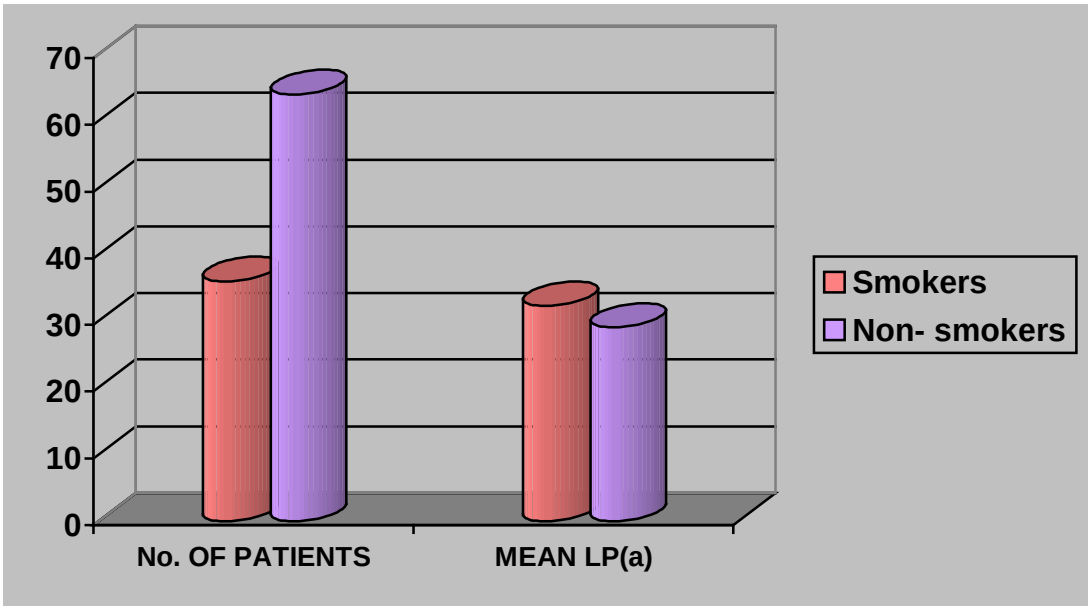


LP(a) AND SMOKING:

The mean serum Lipoprotein (a) level was calculated among the smokers and non smokers. Found to be higher in smokers than among non – smokers which is statistically significant.

Table-9:

SL. NO	RISK FACTOR	NO.OF PATIENTS	MEAN LP(a) mg/dl
1.	Smokers	36	32.30
2.	Non- smokers	64	29.04

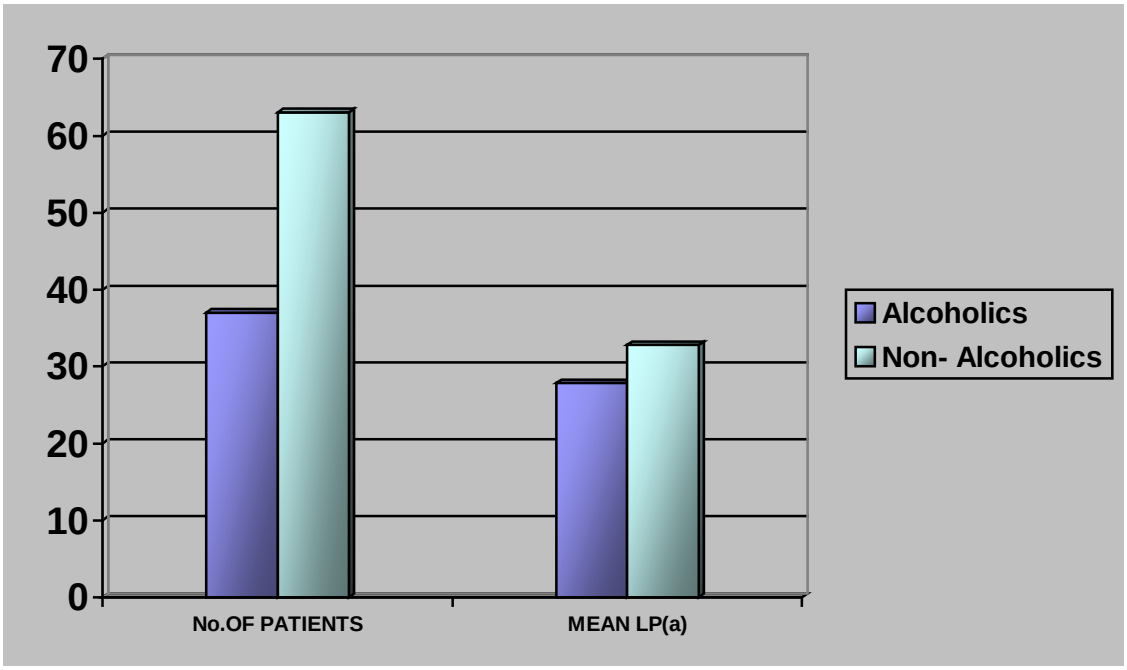


LP(a) AND ALCOHOL:

Analsysis among alcoholics shows that there is no significant correlation between alcohol and serum Lipoprotein (a) levels. Alcoholics have low mean LP(a) levels than Non-alcoholics.

Table-10:

SL. NO	RISK FACTORS	No.OF PATIENTS	MEAN LP(a) mg/dl
1.	Alcoholics	35	27.8
2.	Non- Alcoholics	65	32.8

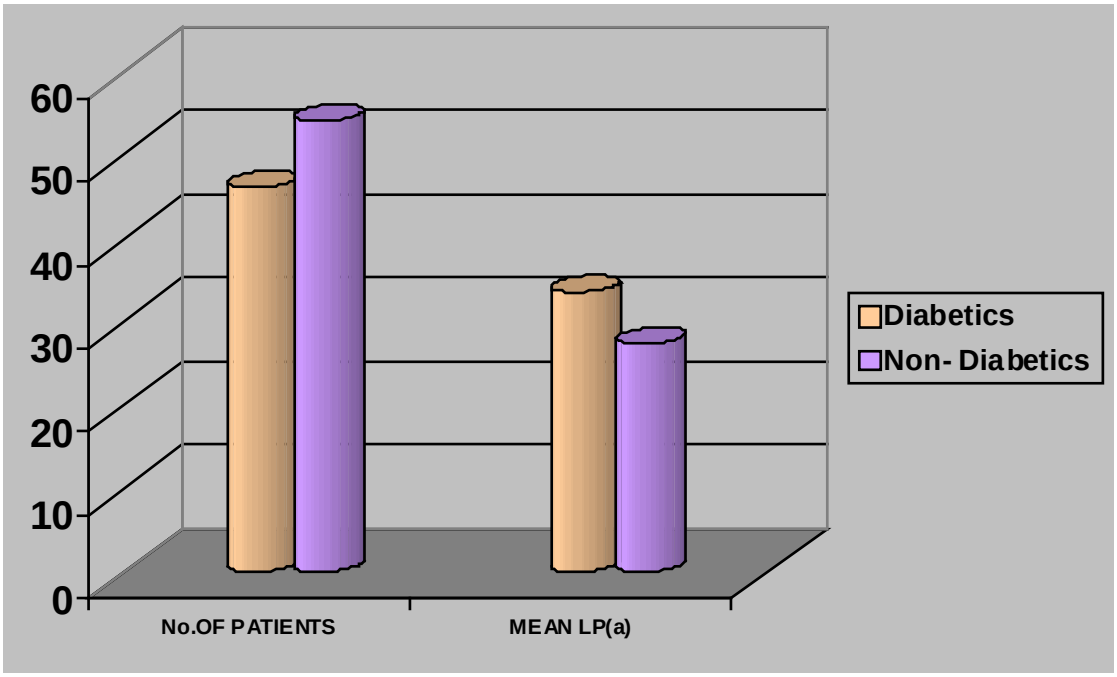


LP(a) AND DIABETES MELLITUS:

The mean LP(a) among the diabetic patients with CAD was found to be higher than the non-diabetics.

Table-11:

SL. NO	RISK FACTORS	No.OF PATIENTS	MEAN LP(a) mg/dl
1.	Diabetics	46	33.50
2.	Non- Diabetics	54	27.31

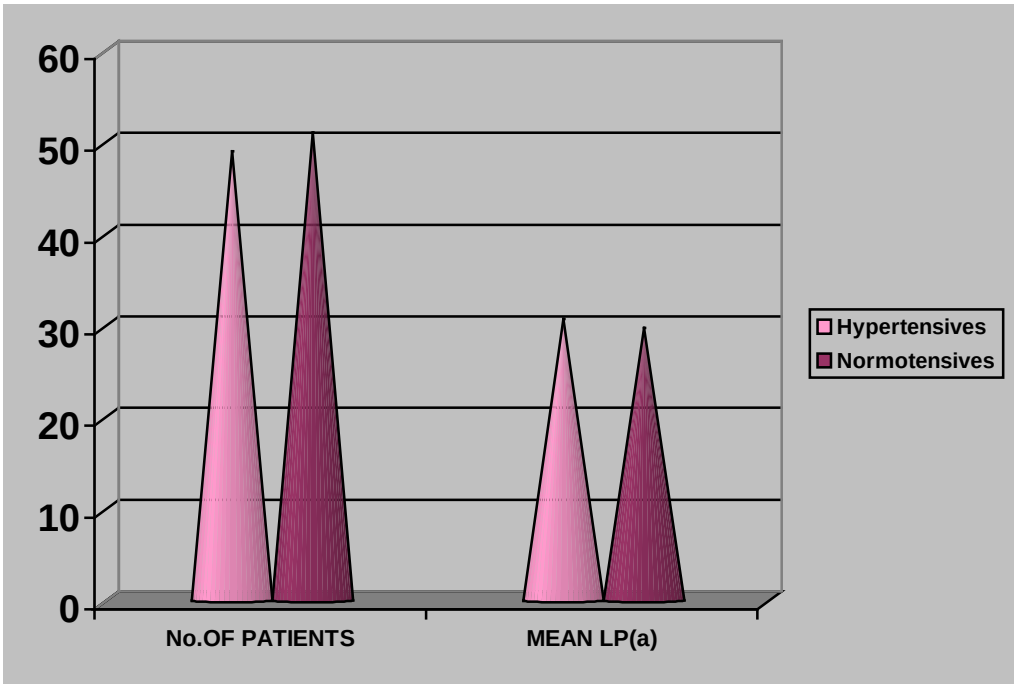


LP(a) AND HYPERTENSION:

No significant difference in mean LP(a) levels were observed between hypertensives and Normotensives.

Table-12:

RISK FACTORS	No.OF PATIENTS	MEAN LP(a) mg/dl
Hypertensives	49	30.2
Normotensive	51	29.7

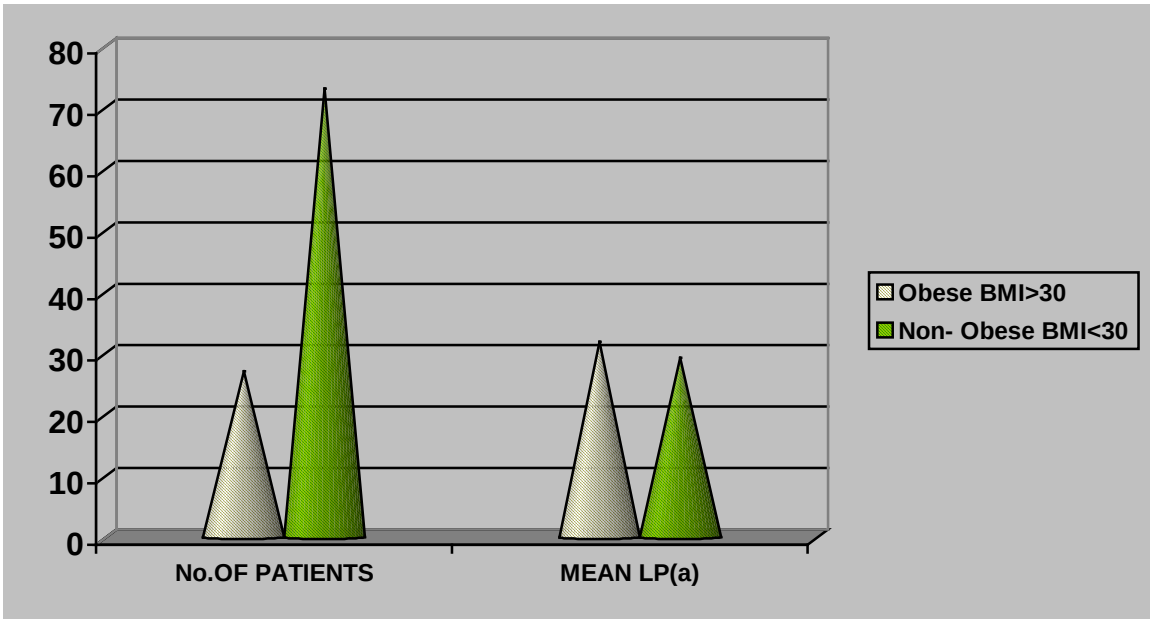


LP(a) AND OBESITY:

The mean LP(a) among the Obese patients with CAD was found to be slightly higher than the Non-obese .

Table-13:

SL. NO	RISK FACTORS	No.OF PATIENTS	MEAN LP(a) mg/dl
1.	Obese BMI≥30	39	31.8
2.	Non- Obese BMI<30	61	29.17

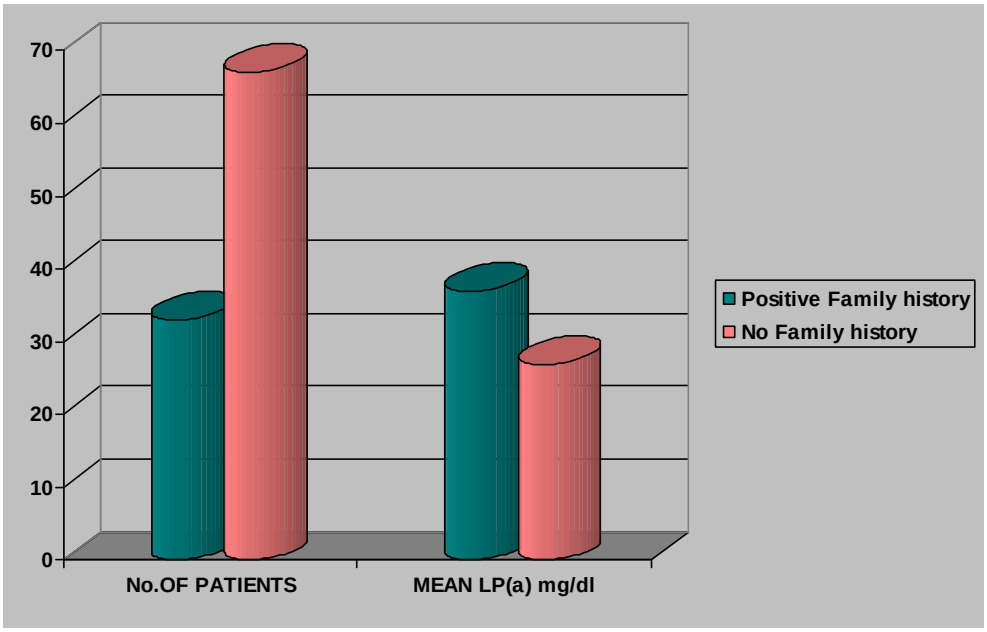


LP(a) AND FAMILY HISTORY OF CAD:

The mean LP(a) level among the patients with positive family history was 37.0 mg/dl which was significantly higher and about 60% of them had LP(a) level >30mg/dl . This showed that there is positive correlation between LP(a) level and patients with positive family history.

Table-14:

RISK FACTORS	No.OF PATIENTS	MEAN LP(a) mg/dl
Positive Family history	33	37.0
No Family history	67	26.8

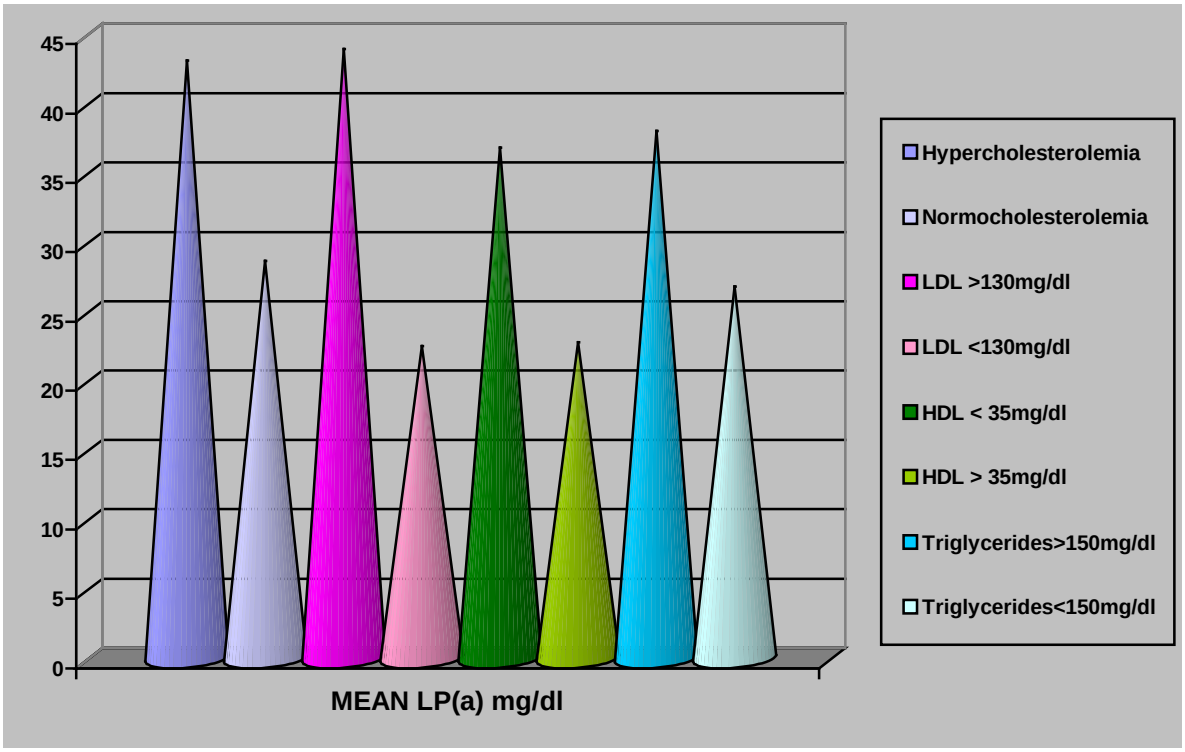


ANALYSIS OF SERUM LP(a) LEVELS WITH THE SERUM LIPID PROFILE:

The mean Serum Lp(a) levels in the patients with normal and abnormal lipid profile values were calculated and tabulated below.

Table-15:

SL.NO	RISK FACTORS	MEAN LP(a) mg/dl
1.	Hypercholesterolemia	43.1
	Normocholesterolemia	28.62
2.	LDL >130mg/dl	43.9
	LDL <130mg/dl	22.51
3.	HDL < 35mg/dl	36.81
	HDL > 35mg/dl	22.8
4.	Triglycerides>150mg/dl	38
	Triglycerides<150mg/dl	26.8



SERUM LP(a) LEVELS WITH THE SERUM LIPID PROFILE

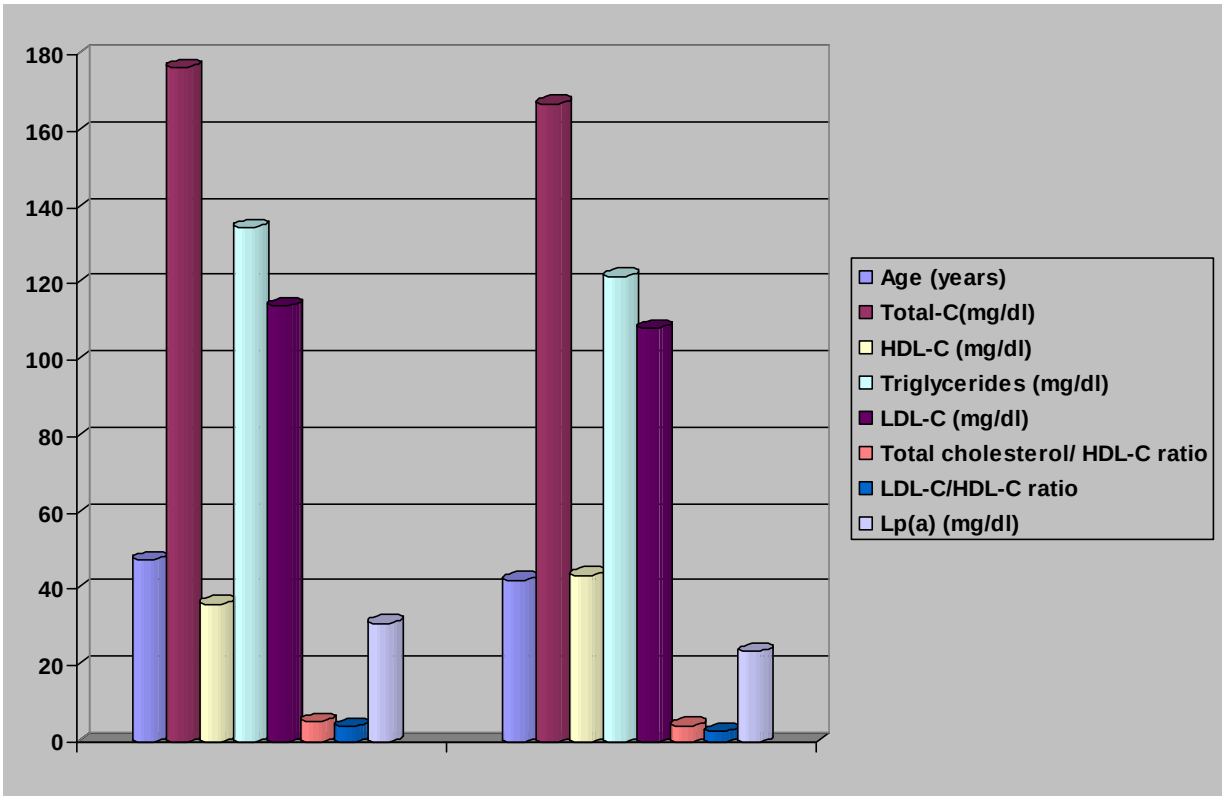
In patients with premature CHD higher mean Lp(a) levels were observed in patients with hypercholesterolemia, high LDL levels, low HDL levels and hypertriglyceridemia than those with normal lipid profile.

COMPARISION BETWEEN CASES AND CONTROLS:

The results obtained from comparing the fasting lipid profile and fasting lipoprotein(a) values in 100 premature CAD cases and 50 controls were as follows.

TABLE-16:

SL.NO	DETAILS	CHD Patients N=100 MEAN VALUES	CONTROLS N=50 MEAN VALUES
1.	Age (years)	**47.6**	**42.22**
2.	Sex(M/F)	**85/15**	**39/11**
3.	Total-C(mg/dl)	**176.5**	**167.1**
4.	HDL-C (mg/dl)	**35.9**	**43.5**
5.	Triglycerides (mg/dl)	**134.7**	**121.8**
6.	LDL-C (mg/dl)	**114**	**108.3**
7.	Total cholesterol/ HDL-C ratio	**5.2**	**4.2**
8.	LDL-C/HDL-C ratio	**3.9**	**2.6**
9.	**Lp(a) (mg/dl)**	**30.98**	**23.58**



Significant difference in mean Lp(a) level was observed between patients and Controls. The mean LP(a) values among the premature CAD patients were found to be higher than in controls**.(30.98 vs23.58)**

The mean values of Triglycerides ,LDL, Total cholesterol, LDL-C, Total-C/HDL-C ratio and LDL-C/HDL-C ratio were found to be higher in patients when compared to controls. Higher percentage of low HDL-C (<35mg/dl) was observed in patients than in controls.

Fig-11 : ECG of a patient showing LBBB with AWMI

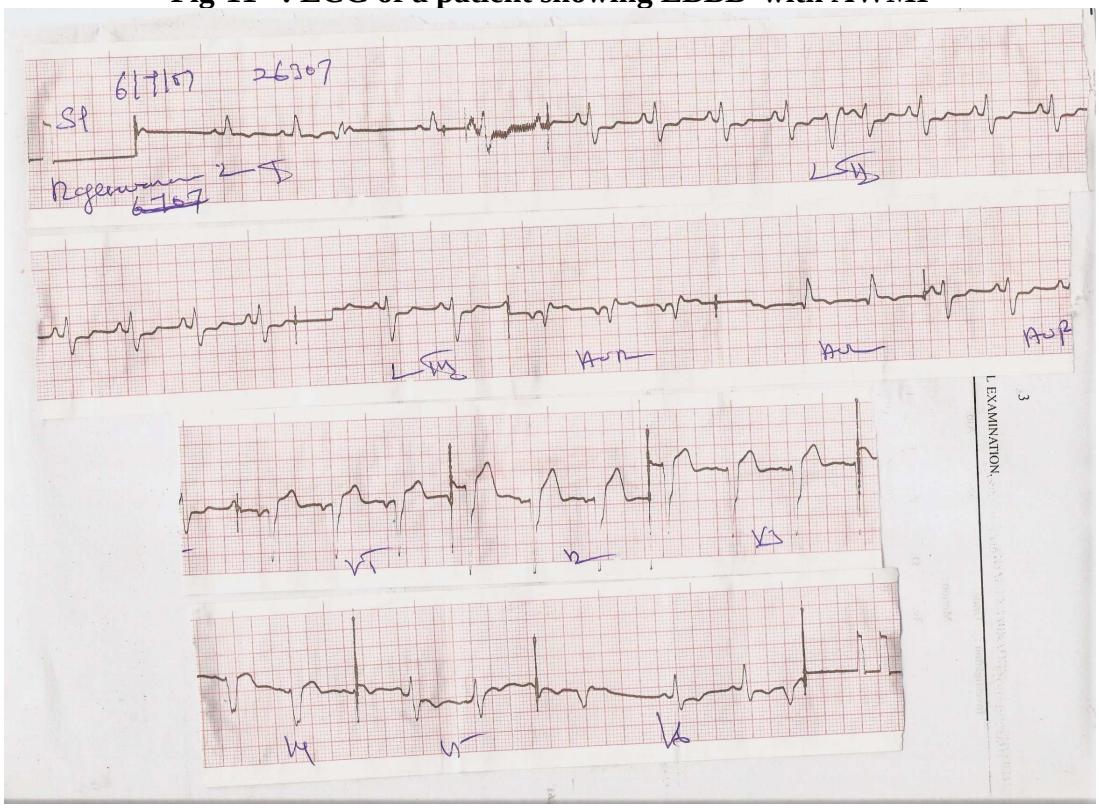


Fig-12:ECG of a patient showiing Anterior wall ischemia

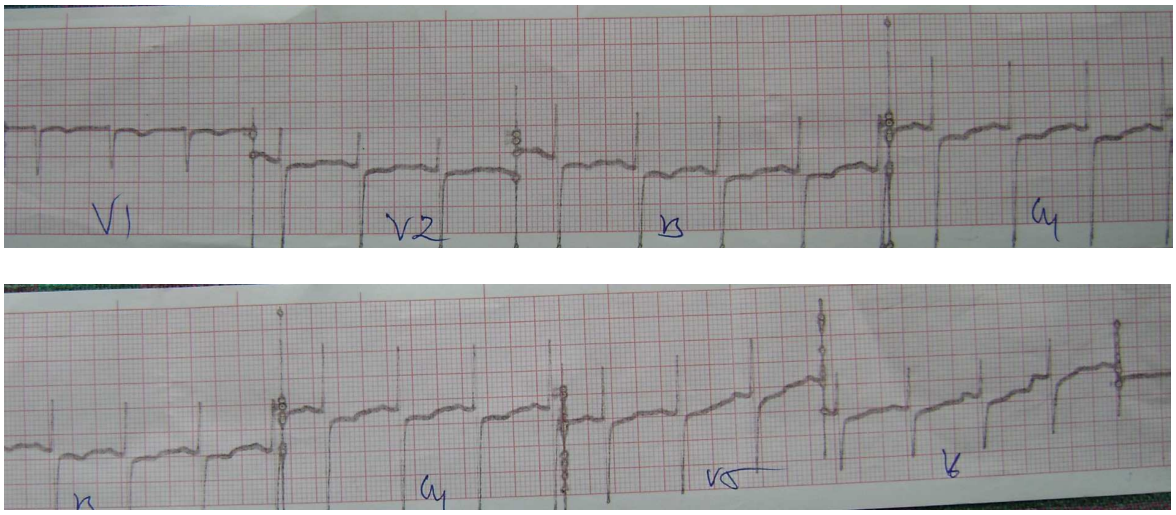
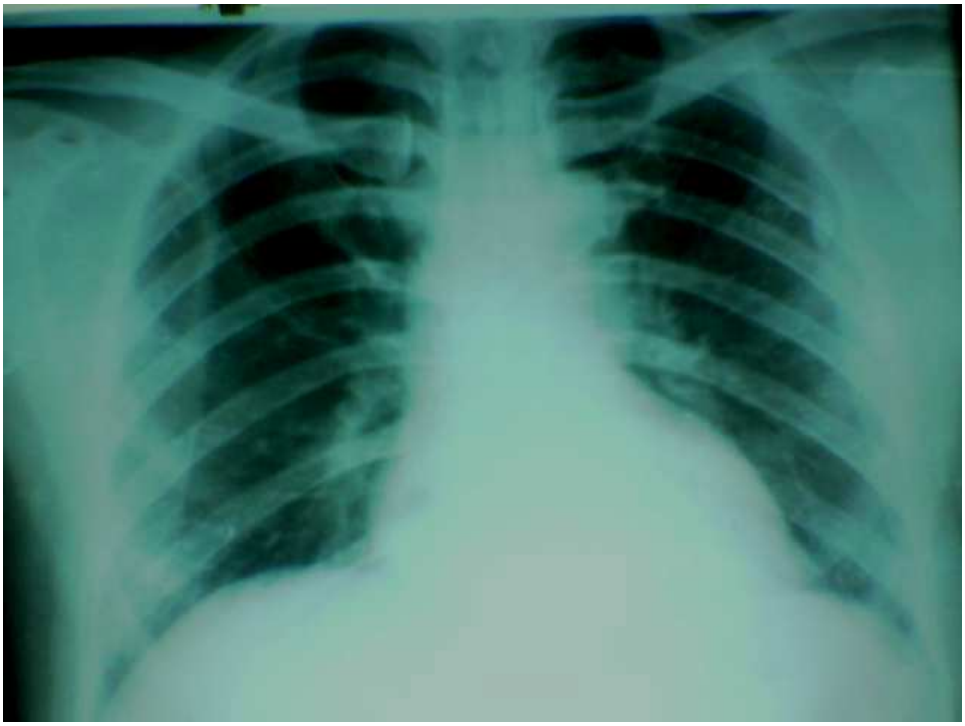
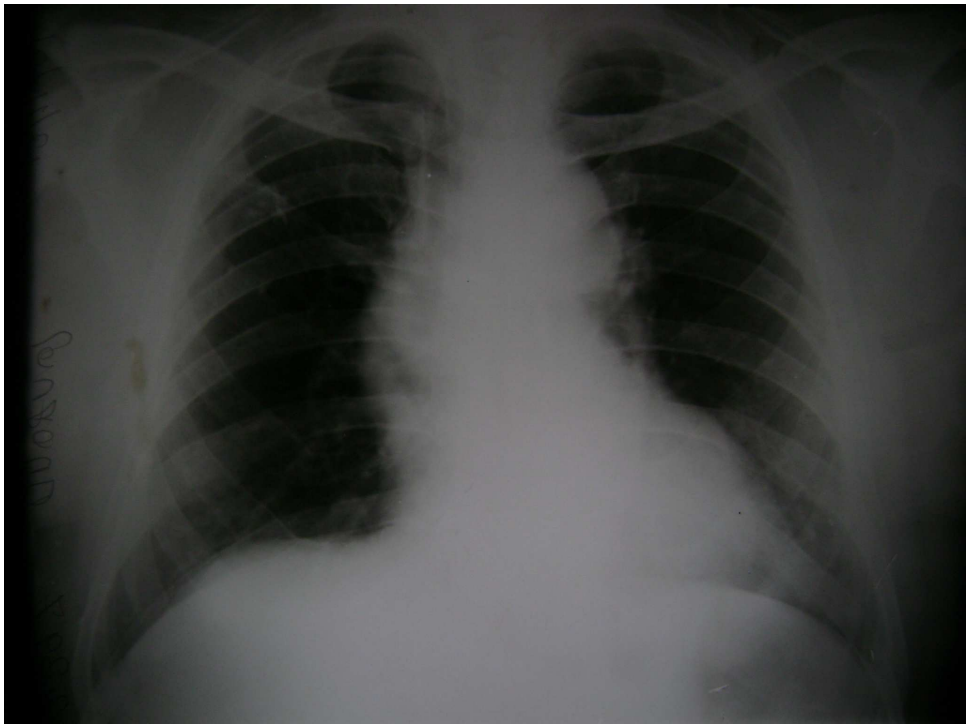


Fig-13:CHEST X-RAY PA VIEW showing cardiomegaly – LVH





DISCUSSION

Higher mean Lp(a) levels were observed in patients than controls and difference was statistically significant. **(30.9vs23.6)**. This is in agreement with earlier studies conducted in India and abroad (89-103).Higher mean levels of Lp(a) were observed in cases than control in studies reported in India which ranged from 12 to 49mg/dl in patients and 8 to 24 mg/dl in healthy controls (91-97). Mean Lp(a) levels in patients and controls in our study were within the range of values reported in earlier Indian studies.

Low levels of HDL-C observed in patients when compared to controls (43.5vs35.9) in the present study is in agreement with the other Indian Study(86). With respect to low levels of HDL-C our study is similar to other studies (86-88).

Increased total-C(134.7vs121.8) and LDL-C(114vs108.3) levels are reported in patients than in controls (88-90). In our study similar findings were observed in patients against controls.

Increased LDL-C/HDL-C ratio(3.9vs2.6) and total cholesterol /HDL ratio(5.2vs4.2)were reported in patients when compared to controls (87,89). Similar observations were drawn in the present study.

IN PREMATURE CAD PATIENTS,

This study showed higher Lp(a) levels in females when compared to males **(40.3vs28.2)** in patients and is in agreement with other reports (101,104,105). Pedreno *et al*. (99) showed no gender differences in Lp(a) levels in both patients and controls. Though influence of sex on Lp(a) is not established in literature and the higher levels of Lp(a) in females than in males may be due to lowering effect of testosterone in males (106) and presence of menopausal status (107) in women with Coronary Artery Disease or may be due to discrepancy in sample size. Further studies are needed to confirm this observation.

The mean Lp(a) levels in different age groups of the patients varies between 22mg and 35mg . No specific age group shows higher LP(a) levels.

Smokers were found to have slightly higher mean LP(a) levels than Non-Smokers in this study **(32.3vs29.04)**. Studies have shown that Elevated blood levels of Lp(a) and cigarette smoking together greatly exacerbate the risk of coronary heart disease. One study suggests that cigarette smoking specifically alters Lp(a) concentrations in the blood.

The mean Lp(a) levels in this study were low in Alcoholics than among the non-alcoholics **(27.8vs32.8)**. Finnish Population based studies have shown that low Lp(a) lipoprotein concentrations may be

one factor explaining low mortality and retarded progression of coronary artery disease in social drinkers.(85)

In this study, mean Lp(a) levels were higher in diabetics than among non-diabetics**(33.5vs27.3).** Mohan *et al*. (7) reported in a study that Lp(a) levels were higher in NIDDM patients with or without Coronary Artery Disease than controls.

No significant difference in mean LP(a) levels were observed between hypertensives and Normotensives**(30.2vs29.7)** in this study. Studies have shown only weak positive correlation of LP(a) with systolic blood pressure.

Higher Lp(a) levels were observed in individuals with a strong family history of Coronary Artery Disease than in those without such history**(37vs27.6)** which is in agreement with other report (108). The disturbance in lipoprotein metabolism is often familial. Studies have shown that LP(a) excess is one of the common lipoprotein abnormalities among the family members.

Lp(a) level is an important determinant of Coronary Artery Disease among patients with familial and non-familial hypercholesterolemia (109). In the present study also higher Lp(a) levels were observed in patients with hypercholesterolemia than normocholesterolemia **(43.1vs28.62)**

Lp(a) levels in our study were high in patients with LDL-C >130 mg/dl than patients having LDL-C <130 mg/dl **(43.9vs22.51).** Other studies (99) reported positive significant association of Lp(a) with LDL-C. In the present study strong positive correlation of Lp(a) with LDL-C was observed. The pathogenicity of Lp(a) is increased with high LDL and vice-versa (110,111)

Our study confirmed positive correlation of Lp(a) with Coronary Artery Disease at >30mg/dl, a cut-off level in South Indian population for risk assessment similar to the earlier studies .

Higher mean values of Lp(a) in the present study may explain higher prevalence of Coronary Artery Disease reported in South Indian population. Females, patients with positive family history of Coronary Artery Disease, Diabetics ,hypercholesterolemia and those with LDLC >130 mg/dl showed higher Lp(a) levels. These findings indicate that these category of patients are at high risk of developing Coronary Artery Disease in future as evidence shows that Lp(a) excess increases the risk of Coronary Artery Disease in future depending on the absence or presence of concomitant risk factors .

This observation suggests that in addition to conventional lipid profile, estimation of Lipoprotein(a) can prove to be a valuable tool in risk assessment of population in general and management of disease in particular.

SUMMARY

Significant difference in mean Lipoprotein(a) level was observed between the premature Coronary Artery Disease patients and controls **(30.98vs23.58) .**

The mean values of serum Triglycerides, LDL, Total cholesterol, LDL-C, Total-C/HDL-C ratio and LDL-C/HDL-C ratio were found to be higher in premature Coronary Artery Disease patients when compared to controls.

In patients with Premature Coronary Artery Disease, higher Lipoprotein(a) levels were observed in female sex, those with family history of Coronary Artery Disease, Smokers, and Diabetics than in male sex, those without family history of Coronary Artery Disease, non-smokers and non-diabetics.

There is no significant difference in mean Lipoprotein(a) levels between hypertensives and Normotensives in premature Coronary Artery Disease patients.

Higher Lipoprotein(a) levels were observed in all premature Coronary Artery Disease patients with hypercholesterolemia, high LDL levels, low HDL levels and hypertriglyceridemia than those patients with normal serum lipid profile.

No significant difference in Lipoprotein(a) levels was observed with respect to age in premature Coronary Artery Disease patients.

Alcoholics had lower levels of serum Lipoprotein(a) compared to the Non-alcoholics with coronary artery disease.

CONCLUSION

- **High serum Lipoprotein (a) levels are associated with premature coronary artery disease.**

- **There is a strong positive correlation of High serum Lipoprotein (a) levels with High serum LDL levels and those with positive family history.**

- **High serum Lipoprotein (a) levels are seen in patients with Smoking and Diabetes.**

- **There is no correlation of High serum Lipoprotein (a) levels with respect to age and Hypertension.**

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PROFORMA

NAME:

AGE: **SEX: M/F**

OCCUPATION:

I.P.NO:

DIAGNOSIS:

COMPLAINTS*:*

HISTORY OF PRESENT ILLNESS:

CHEST PAIN

PALPITATION

DYSPNOEA

SYNCOPE

PND

ORTHOPNOEA

PAST HISTORY: **DIABETES/ HYPERTENSION / CAD**

PERSONAL HABITS: **SMOKING / ALCOHOL**

FAMILY HISTORY OF CAD :

DIET: **VEG/NONVEG/MIXED**

TREATMENT HISTORY: **DRUG INTAKE**

GENERAL EXAMINATION:

- **OBESITY :**

- **DYSPNOEA :**
- **CYANOSIS :**
- **CLUBBING :**
- **PITTING PEDAL EDEMA :**
- **XANTHALESMA :**
- **TENDON XANTHOMAS :**
- **ARCUS SENILIS :**
- **PULSE :**
- **BLOOD PRESSURE :**
- **WAIST CIRCUMFERENCE :**

HEIGHT: **WEIGHT:**

BMI:

WAIST:HIP RATIO:

CARDIOVASCULAR SYSTEM:

APICAL IMPULSE **S1** **S2** **S3**

PERICARDIAL RUB

PERIPHERAL VASCULAR SYSTEM:

RESPIRATORY SYSYEM:

ABDOMEN:

CENTRAL NERVOUS SYSTEM:

INVESTIGATION:

URINE ROUTINE :

BLOOD SUGAR :

BLOOD UREA :

SERUM CREATININE:

FASTING LIPID PROFILE:-

TOTAL CHOLESTEROL: mg%

TGL: mg%

HDL: mg%

LDL: mg%

SERUM FASTING LIPOPROTEIN(a) :

ELECTROCARDIOGRAM:

CHEST X-RAY PA VIEW:

ECHOCARDIOGRAM:

MASTER CHART

S.No	Name	IP No	Age	Sex	Occpn	Smoking	Alcohol	DM	SHT	Fam H/O	BMI	W.H.R	LP(a)	LDL	HDL	TGL
1	Ramaswan	13608	48	M	Coolie	+	+	+	+	-	32	1.08	35	130	38	100
2	Karuppan	15740	55	M	Coolie	-	-	-	-	+	23	0.8	10	117	39	110
3	Shekar	15826	41	M	Coolie	-	-	+	+	+	31	1.1	40	142	32	180
4	Kannan	16195	50	M	Coolie	+	+	-	-	-	31	1.02	30	182	34	170
5	Palaniswar	16201	52	M	Coolie	+	+	-	+	-	30	1.04	33.8	135	33	148
6	Karuppusa	16235	53	M	Coolie	+	-	+	-	-	31	0.9	36	171	34	150
7	Selvaraj	16326	44	M	Coolie	-	-	-	+	+	28	0.9	21	136	35	145
8	Moorty	16538	52	M	Coolie	+	-	+	+	+	32	1.2	37	154	36	140
9	Rajan	16773	50	M	Coolie	-	-	-	+	-	27	1.1	8	86	40	120
10	Arumugam	17068	39	M	Coolie	-	-	+	+	-	30	1.1	35.1	188	40	160
11	Natarajan	17419	44	M	Coolie	+	-	-	-	-	26	0.8	37	157	50	170
12	Anandkum	17883	45	M	Coolie	+	-	+	+	+	31	0.99	34.3	132	33	155
13	Ganesan	18491	40	M	Coolie	-	-	+	+	-	29	0.8	7	102	46	110
14	Ranjith	18572	28	M	Coolie	+	-	-	-	-	27	0.8	38.3	141	32	158
15	Selvaraj	19067	55	M	Coolie	-	-	+	+	-	29	0.9	11	70	46	120
16	Velumani	19589	40	M	Coolie	-	-	-	-	-	24	0.8	41	130	32	138
17	James	20146	43	M	Coolie	-	+	+	+	-	33	1.11	9	119	40	125
18	Chandran	20786	50	M	Coolie	+	-	-	-	-	29	0.97	9	65.8	40	131
19	Duraiswam	21831	54	M	Coolie	-	-	+	+	+	31	1.05	22	97	36	135
20	Eswaran	23608	40	M	Coolie	-	+	-	-	-	23	0.76	21	118	30	158
21	Selvan	23710	45	M	Coolie	+	¯	+	+	+	33	1.18	9	113	35	110
22	Vadivel	23909	45	M	Coolie	+	+	+	+	-	32	1.19	10	110	36	121
23	Paramasiv	24547	47	M	Coolie	-	-	+	+	-	31	1.1	30	187	34	145
24	Senthil	24528	29	M	Coolie	+	+	+	+	+	30	1	10.4	68	34	120
25	Karuppan	2E+05	40	M	Coolie	+	+	-	-	-	28	0.8	9.3	81.4	38	118
26	Shanmuga	28273	53	M	Coolie	-	-	-	-	-	22	0.7	10	87	35	110
27	Loganathai	28584	49	M	Coolie	-	+	+	+	-	33	1.21	29	136	56	152
28	Raju	29390	50	M	Coolie	-	-	-	+	-	31	1.11	30	115	32	148
29	Nanjamal	30530	40	M	Coolie	+	+	-	-	+	24	0.8	30.6	134	35	159
30	Gopal	30775	50	M	Coolie	-	-	+	+	-	28	0.91	9	93.6	34	102
31	Subbamal	40634	65	F	Coolie	-	-	-	-	+	28	0.6	9	100	36	108
32	Krishnama	4E+05	60	F	Coolie	-	-	+	+	-	30	0.9	7	89	38.4	110
33	Mohanraj	41876	41	M	Coolie	+	+	+	+	+	23	0.8	36	184	36	130
34	Siva	52396	38	M	Coolie	+	+	-	-	-	33	1.2	10	107	33	125
35	Jayaprakas	42674	43	M	Coolie	+	¯	+	+	-	27	0.9	11	85.4	38	128
36	Dhramaraj	43656	54	M	Coolie	+	-	-	-	-	29	0.9	10	70	39	160
37	Palaniswar	44415	51	M	Coolie	+	+	+	+	-	25	0.7	29	131	36	128
38	Batsha	46494	55	M	Coolie	+	+	-	-	-	34	1.31	30	130	34	118
39	Nanjappan	24156	54	M	Coolie	+	+	-	-	+	21	0.7	10.4	90	34	102
40	Palaniswar	42962	40	M	Coolie	-	+	+	+	-	24	0.6	69.8	84.8	38.8	145
41	Kittan	53756	50	M	Coolie	-	-	-	+	-	29	0.92	70.5	149	36	142
42	Ramdoss	53382	50	M	Coolie	-	-	-	-	-	21	0.6	11.2	41.6	31	130
43	Kaliyamma	55560	60	F	Coolie	+	-	-	-	-	29	0.9	126	128	50	128
44	Pattammal	54520	43	F	Coolie	-	-	+	-	+	30	0.9	9.5	84.6	30	120
45	Rajendran	56395	46	M	Coolie	-	+	-	-	+	22	0.6	16.8	31.6	41	170
46	Valliyamm	52241	55	F	Coolie	+	-	-	-	-	28	0.8	126	143	48	141
47	Thangaraj	56378	47	M	Coolie	-	+	-	-	+	27	0.9	14.4	108	31	
48	Ayyasamy	56451	40	M	Coolie	-	-	-	-	-	28	0.17	22.3	76	41	

49	Noormuhai	53901	54	M	Coolie -	-	-	-	-	29	0.81	11.2	135	42	
50	Subbalaksl	59098	42	F	Coolie +	-	-	-	+	25	0.9	39.9	89.8	42	
51	Samakaya	44064	53	M	Coolie -	-	+	-	+	34	0.91	131	192	30	190
52	Manasevar	59148	55	M	Coolie +	+	-	-	-	29	0.81	33	119	31	102
53	Rajan	55148	51	M	Coolie -	-	+	+	+	28	0.7	96	132	22	157
54	Karuppusa	60585	55	M	Coolie -	-	-	-	-	31	1.1	35.2	113	30	110
55	Hari krishn	60434	55	M	Coolie +	+	+	+	+	34	1.31	104	130	34	160
56	ELSE	56001	55	F	Coolie -	-	+	+	+	29	0.8	123	129	34	198
57	Manikanda	60532	40	M	Coolie -	-	-	-	-	30	1.1	22	128	33	145
58	Shekbajan	62239	55	M	Coolie -	-	+	-	-	28	1	78	113	34	115
59	Vadivel	62198	55	M	Coolie -	-	+	-	-	29	0.89	9	122	36	151
60	Palaniswar	62062	43	M	Coolie +	+	+	-	+	29	0.81	30	114	34	102
61	Selvan	62055	45	M	Coolie -	+	+	-	-	33	0.81	8	76.6	38	100
62	Ganesan	62480	31	M	Coolie -	-	-	+	-	32	1.7	57	132	30	153
63	Ranganath	62306	35	M	Coolie +	+	-	-	+	25	0.75	9	72.2	38	104
64	Jeganadan	62229	55	M	Coolie -	+	-	-	-	26	0.6	7	78.8	39	101
65	Shaigabee	62285	45	F	Coolie -	-	-	+	+	29	0.88	22	84.2	30	154
66	Periyaswar	61772	55	M	Coolie +	+	+	+	-	27	1.1	10	67.4	38	103
67	Karuppan	61806	45	M	Coolie -	+	-	-	-	23	0.71	8	91	37	110
68	Thangavel	61865	55	M	Coolie -	-	+	+	+	31	0.95	21	133	31	118
69	Karuppan	6E+05	50	M	Coolie -	-	+	+	-	30	0.94	29	182	33	158
70	Khandaraj	61998	42	M	Coolie -	+	+	+	-	33	1.38	14	73.6	40	107
71	Malikathiya	61692	53	M	Coolie -	-	-	+	-	30	1.1	36	187	30	100
72	Umjalalma	61894	65	F	Coolie -	+	-	-	+	21	0.8	11	77	39	110
73	Shankar	61762	55	M	Coolie -	+	-	-	-	28	0.8	12	79	38	115
74	Balan	61764	50	M	Coolie -	-	-	+	+	29	0.9	27	111	34	151
75	Pandiyan	61721	39	M	Coolie +	+	-	-	-	27	0.85	10	91	40	150
76	Palaniswar	61535	35	M	Coolie +	-	+	+	-	31	1.1	32.7	100	30	158
77	Kuppuraj	61587	50	M	Coolie +	+	+	+	-	26	1.81	8	91.4	39	103
78	Ayyavu	61613	50	M	Coolie -	-	-	-	+	27	0.7	36	100	31	159
79	Raju	61644	48	M	Coolie +	-	+	+	-	34	1.2	34.8	112	34	158
80	Kaliyappan	61677	40	M	Coolie -	+	-	-	-	30	1.2	10	72	38	100
81	Ummari	60891	50	F	Coolie -	-	+	+	-	31	1.91	10	82.6	34	117
82	Raju	61493	50	M	Coolie -	-	-	-	+	21	1.91	37	105	33	159
83	Subramani	615	55	M	Coolie -	-	+	+	-	25	0.9	10	131	34	151
84	Premkuma	61514	47	F	Coolie -	-	+	+	-	26	0.8	20	118	31	157
85	Palaniappa	60788	55	M	Coolie -	-	-	-	+	24	0.9	31	83	33	120
86	Thirumalai	61184	50	M	Coolie +	-	+	-	-	20	0.7	33.1	82.8	33	121
87	Muthu	61263	54	M	Coolie -	-	+	+	-	23	0.71	11	81.4	37	158
88	Manikanda	61270	33	M	Coolie -	+	-	-	+	21	0.6	36	137	31	160
89	Rajan	61273	40	M	Coolie +	-	+	+	-	25	0.85	35	147	34	145
90	Sarojini	60737	50	F	Coolie -	-	-	-	-	27	0.79	10	72	38	100
91	Saayed Sh	60851	52	M	Coolie -	+	-	+	-	28	0.71	8	124	34	116
92	Saminatha	60873	23	M	Coolie +	-	-	+	+	21	0.7	35	125	31	118
93	Umusalma	60894	60	F	Coolie -	-	-	-	+	27	0.9	36	116	30	120
94	Synbal	60986	48	M	Coolie -	+	-	+	-	30	0.9	10	77	38	100
95	Ganesan	61049	35	M	Coolie -	-	-	-	-	29	0.9	35.6	195	30	125
96	Ramaswan	61119	52	M	Coolie -	-	-	-	-	27	0.8	37	169	31	148
97	Saraswathi	61124	55	F	Coolie -	-	+	+	-	31	1.1	21	142	34	140
98	Saradhima	61623	55	F	Coolie -	-	+	-	-	31	1.1	35.2	131	30	110
99	Shanmuga	61985	30	M	Coolie -	-	+	-	-	30	1.08	58	110	30	200

100	Gandhimaı	63256	48	M	Cooli	-	-	+	+	+	33	0.8	85.7	135	31	118

Total Chol	TC/HDL	LDL/HDL	ECG	CXR	ECHO
198	5.21	3.42	AWMI	WNL	LVF
178	4.56	3	LWI	WNL	WNL
210	6.5	4.43	AWI	WNL	N
250	7.35	5.35	IWI	WNL	N
198	6	4.093	AWMI	cardiomegaly	LVD
241	7.08	50.2	IWI	N	N
200	5.71	3.88	UA	N	N
208	5.77	4.2	IWMI	N	LVF
150	3.75	2.15	AWMI	N	N
260	6.5	4.7	NSIEM	N	N
241	4.82	3.14	UA	N	N
196	5.93	4	AWMI	N	LVD
170	3.69	2.21	AWMI	cardiomegaly	LVD
245	7.6	4.4	UA	N	N
140	3.04	1.52	IWI	N	LVF
190	5.93	4.06	AWMI	cardiomegaly	LVF
146	3.65	2.97	LWI	N	N
138	3.45	1.7	UA	N	N
160	4.44	2.69	AWMI	N	N
180	6	3.93	ASMI	cardiomegaly	LVD
170	4.85	3.22	UA	N	N
175	4.86	3.02	UA	N	N
250	7.35	5.5	UA	N	N
130	3.4	1.74	AWI	N	N
140	4	2.33	IWI	N	N
145	2.58	1.55	IWI	N	N
198	6.1	4.27	ASMI	N	N
180	5.14	3.28	ASMI	cardiomegaly	LVD
200	5.88	3.94	IWMI	N	N
150	4.16	15.5	UA	N	N
161	4.2	2.56	NSIEM	N	N
145	4.02	2.47	AWI	N	N
243	7.36	5.57	ASMI	cardiomegaly	LVD
170	4.47	2.81	IWI	N	N
150	3.84	2.18	IWI	N	N
138	3.83	1.94	IWI	N	N
190	5.58	3.85	AWMI	N	N
188	5.52	3.82	ASMI	N	N
150	3.84	2.29	UA	N	N
148	4.11	2.43	IWI	N	N
208	6.7	4.7	IWI	N	N
112	2.24	0.82	ASMI	cardiomegaly	LVD
200	6.66	4.7	IWMI	N	N
174	4.24	2.1	IWI	N	N
112	2.33	0.64	IWI	N	N
200	6.75	4.6	UA	N	N
175	4.2	2.53	NSIEM	N	N
142	3.38	1.8	WIW	N	N

201	4.78	2.97	ASMI	N	N
160	3.8	2.14	ASMI	N	N
260	8.6	6.4	LWI	N	N
170	5.48	3.93	AWHI	cardiomegaly	LVD
189	8.45	6	AWHI	cardiomegaly	LVD
165	5.5	3.76	LWMI	cardiomegaly	LVD
196	5.76	3.84	UA	N	N
203	5.97	3.79	UA	N	N
190	5.75	3.87	LWI	N	N
170	5	3.32	ASMI	N	N
188	5.22	3.88	ASMI	N	N
168	4.94	3.32	LWI	N	N
135	3.97	2.02	LWI	N	N
193	6.43	4.4	IWI	N	N
131	3.44	1.89	ASMI	cardiomegaly	LVD
138	3.53	2.02	ASMI	cardiomegaly	LVD
145	4.83	2.8	IWI	N	N
126	3.31	1.76	LWI	N	N
140	3.78	2.45	ASMI	N	N
188	6.06	4.29	ASMI	N	N
247	7.48	5.51	ASMI	N	N
135	3.75	1.84	ASMI	N	N
249	8.3	6.23	LWI	N	N
138	3.5	1.97	AWI	N	N
140	3.68	2.07	IWI	cardiomegaly	LVD
175	5.14	3.23	LWI	N	N
161	4.02	2.27	ASMI	N	N
162	5.4	3.34	ASMI	N	N
141	3.61	2.32	IWHI	N	N
163	5.25	3.22	AWMI	N	N
178	5.23	3.29	UA	N	N
130	3.42	1.89	NSIEM	N	N
140	4.11	2.44	NSIEM	N	N
170	5.15	3.18	NSIEM	N	N
165	4.85	2.94	AWMI	N	N
180	5.29	3.8	IWMI	N	N
140	4.24	2.51	IWMI	N	N
151	4.57	2.51	US	N	N
150	4.05	2.18	NSIEM	N	N
200	6.45	4.41	LWI	N	N
210	6.17	4.32	IWMI	N	N
130	3.42	1.89	ASMI	N	N
181	5.32	3.64	IWI	N	N
180	5.8	4.03	UA	cardiomegaly	LVD
170	5.66	3.86	NSIEM	N	N
135	3.55	2.02	UA	N	N
250	8.33	6.5	ASMI	N	N
231	7.45	5.45	ASMI	N	N
204	6	4.17	ASMI	N	N
180	6	4.36	UA	cardiomegaly	LVD
180	6	3.66	NSIEM	N	N

190	6.12	4.35	LWI	N	N

S.NO	NAME	AGE	SEX	LDL	HDL	TG	TOTAL CH	VCDL	TC/HDL	LDL/HDL	Lp(a)
1	karuppusamy	50	M	126	28	130	180	26	6.43	4.5	30
2	Raman	40	M	75mg	52	116	150	23.2	2.59	1.44	13
3	Kumar	45	M	75	50	115	148	23	2.96	1.5	12
4	Mallika	51	F	76.8	50	116	150	23.2	3	1.54	14
5	Rangammal	45	F	66	40	120	130	24	3.4	1.65	15
6	Arivinda	28	M	75.6	52	122	152	24.4	2.35	1.442	17
7	Palaniyammal	50	F	103.4	43	123	171	24.6	3.97	2.39	18
8	Kuppan	50	M	144.4	33	138	215	27.6	6.515	4.36	40
9	Karuppayan	53	M	136	38	140	202	28	5.32	3.57	38
10	Gandhi	38	F	93.2	50	125	179	35.8	3.58	1.86	20
11	Palanisamy	48	M	113.8	41	126	180	25.2	4.39	2.78	17
12	Govindhan	40	M	94.4	42	118	160	23.6	3.8	2.23	18
13	Kuppathal	50	F	97	42	120	163	24	3.79	2.3	15
14	Rangamn	53	M	139.2	44	121	208	24.8	4.72	3.16	50
15	Masilamani	42	M	107.2	46	124	178	24.8	3.87	2.32	20
16	Kittan	50	M	105mg	40	125	170	25	4.25	2.625	19
17	Marriyammal	55	M	149.4	38	138	215	27.6	5.66	3.92	75
18	Gathi	28	F	117	59	120	175	24	3.39	1.98	39
19	Porravathy	38	F	127	37	130	200%	26	4.87	3.43	49
20	Joeshp	45	M	104.4	38	128	168%	25.6	4.42	2.73	57
21	Yooasaj	45	M	109.4	72	118	198	23.6	4.16	2.6	13
22	Manikkam	50	M	154.4	32	118	210	23.6	6.56	4.81	33
23	Nattayan	40	M	97	38	125	160	25	4.34	2.55	19
24	Lakshmi	50	F	91.4	48	128	165	25.6	3.43	1.917	14
25	Badaiyappan	45	M	102	48	100	170	20	3.54	2.125	17

26	Balan	40	M	102.8	52	116	178	23.2	3.42	1.96	18
27	Ramayappan	45	M	138.2	38	119	200	23.8	5.26	3.63	19
28	Selvaraj	30	M	117.4	37	118	178	23.6	4.8	3.16	14
29	Ayyasamy	20	M	94	44	110	160	22	3.6	2.13	13
30	Govindarajan	37	M	138	36	130	200	26	5.56	3.8	35
31	Kuppammal	50	F	132.4	44	118	200	23.6	4.54	3	36
32	Eswaran	40	M	130	36	140	194	28	5.38	3.61	17
33	Rangappan	48	M	127.4	35	138	190	27.6	5.42	3.62	18
34	Palaniyappan	43	M	118	36	129	180	25.8	5	3.27	17
35	Meena	25	F	95.8	39	126	160	25.2	4.1	2.46	19
36	Venkatachalam	36	M	95.4	46	118	165	23.6	3.59	2.06	14
37	Christopher	30	M	87.4	50	118	161	23.6	3.22	1.74	12
38	mantha	41	F	109	45	120	178	24	3.96	2.42	30
39	Ahakbar	38	M	102	39	123	165	24.6	4.8	2.615	13
40	Abraham	51	M	104.4	35	128	168	25.6	4.71	2.97	11
41	sivasamy	50	M	151.8	32	131	210	26.2	6.56	4.93	35
42	senthilkumar	30	M	119	58	116	200	23.2	3.45	2.05	39
43	Murugaran	43	M	79	47	118	150	23.6	3.19	1.68	17
44	Ramasamy	44	M	72	58	110	152	22	2.62	1.24	15
45	Ismayil	40	M	77.4	52	108	151	21.6	2.9	1.48	18
46	Manikandan	43	M	93	45	106	160	21.2	3.55	2.06	14
47	Narayanan	38	M	98.4	39	118	161	23.6	4.13	2.51	11
48	Mariyappan	49	M	156	28	120	208	24	7.14	5.57	38
49	Kuttiyappan	48	M	101	42	121	108	24.2	4	2.4	16
50	Karthikeyan	23	M	58.4	60	108	144	25.6	2.4	0.96	18